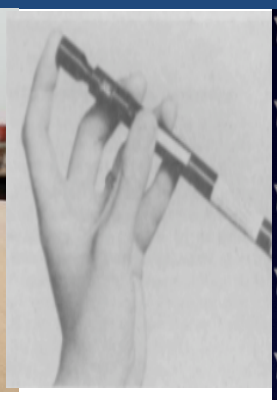
SPIN

Medical devices, medical research and healthcare systems

Notes, thoughts, and anecdotes

David Wyper



Instruction Manual

The main objective behind this book is to raise money for research into the treatment of brain conditions. You might want just to make a donation and not bother with the book, but it's there if you want it, and there are bits that you might be interested in. Did you know that medical ultrasound scanning was first developed in Glasgow, or that the pioneering work to produce the first insulin injection pen took place at the Southern General Hospital? Would you like to understand a bit more about how scanners work and what they are used for? Are you frustrated by bureaucracy and interested in its effect on the NHS? Is there anything that can be done about this? Would you like to know a bit about current research into brain disorders? The challenges facing medical researchers are infinite, but progress is being made in many fields. The book looks into studies in stroke, multiple sclerosis, Parkinson's Disease, brain cancer and several other conditions. How is research organised, and where does the money come from? The book touches on these issues, and there are also a few lighthearted stories to brighten it up at bit. You could read it from cover to cover or just dip into bits before you put this lights out. You might want to find out why the title is SPIN, and you must have a look at the illustrations, courtesy of students at Glasgow Kelvin College.

If you haven't already done so, you can donate to brain research at
http://mydonate.bt.com/events/brain/469724

Many of the examples of working life in the NHS and universities are taken from personal experience. It would be very interesting to compare those with your experiences wherever you work, whether in the public sector or the private sector. You can let me know by emailing dave.wyper@glasgow.ac.uk.

Dedications

Einstein wrote about Brownian motion. This describes the random paths taken by particles in a fluid as they bounce around. I have bounced around medical science, and in so doing have had the privilege of working with colleagues who were excellent scientists or doctors, and also fascinating people; caring and dedicated professionals. Some are mentioned by name but the majority are like those named in the credits that flash past far too quickly to read at the end of a film. Workplace colleagues are the making or the breaking of many careers. When you retire it's perhaps the people rather than the work that you miss most. This short book is to say thank you to you all.

I'd also like to dedicate the book to two special individuals. My colleague Aled Evans died far too early from a brain tumour and my friend and running soulmate Hugh Wilson died as a result of an accident while cycling to work. Both are seldom far from my thoughts.

CONTENTS

PROLOGUE

It's 7:15am. I lace up my running shoes and head out. It's the dawn of a new day and the sun is throwing my long shadow westward. After a couple of miles, I leave the back streets of suburbia and head into parkland and over golf courses. Here the running surface is more forgiving, and the backdrop gives you a sense of being at one with nature. I sense that I'm being watched. Probably rabbits and foxes. Hmm, I like this! In what felt like a few minutes, but was actually just over half an hour, I arrive at work. What a great way to start the day. I feel good. I'm wide-awake. After a quick shower I'm ready to face whatever challenges are thrown at me.

It's 7:15am. I lace up my running shoes and head out. Oh bugger. It's freezing, and horizontal rain makes progress difficult. It's too dark to navigate a path through the park and so pavements are the only option. Bugger. Why did that driver have to splash through a puddle and leave me filthy as well as soaked? Why am I doing this? I must be crazy. In what felt like an hour, but was actually just over half an hour, I arrive at work. I've made it. Undefeated by the weather. What a great way to start the day. I feel good. I'm wide-awake. After a quick shower I'm ready to face whatever challenges are thrown at me.

It's 5:30pm. Time to go home. I lace up my running shoes and head into the evening. There is still warmth in the air. It wasn't the best day to be working indoors, but at least I'll catch the tail end of the sunshine. There are still a few golfers on the course, but they don't mind runners as long as we don't disturb them and stick to the perimeter. There's no traffic congestion, and no crazy driving – apart from that bloke on the 4th tee. My mind is as free as a bird. What a great way to unwind. I feel good. I might even add on an extra few miles. When I arrive home, I'm wide-awake, fresh and ready for a quick shower and a relaxing evening.

It's 5:30pm. Time to go home. I lace up my running shoes and head into the evening. We heard the rain battering off the roof for most of the afternoon and it's still pouring down. Is this a good idea? Well, once you're completely soaked you can't get any wetter. Pity it's dark and I've to take the longer route alongside the roads. I wonder why the traffic has built up? Ah! The road under the bridge has flooded again. I bet the pavement is flooded as well. Yes, it is. I'll have to take care to avoid the potholes. There are always potholes, but when it's dark and flooded they're hard to spot and you have to rely on memory. Having to focus on footsteps can be quite relaxing. My mind is free as a bird. When I arrive home, I'm wide-awake, fresh and ready for a quick shower and a relaxing evening.

For many years that was the start, and the end, of my working day. What about the bits in the middle? This diary recounts some of these. It's not necessary to read from cover to cover. There's no plot, so you can pick and choose. Some might just want to read the sections about the work of the Department of Clinical Physics in Glasgow, or SINAPSE, one of the academic groups helping to join up medical imaging research in Scottish Universities. Some might want to go through the *how do scanners work* sections, and others might know this backwards. Some might be interested in my thoughts about organisation within politically challenged settings like the NHS, and how we might tackle the increasing burden of bureaucracy that is smothering productivity.

I'm not a celebrity. I'm a medical physicist, and this is not the best route to fame or notoriety. I didn't think of writing about my forty-seven years in this field until I came across *Iron in the Blood*, by Richard Morris [1]. He had worked in the railway industry for forty-two years and so had experience of the many reinventions of the rail networks. I went through seven reorganisations of the healthcare network and that set me thinking that a reflection on some of the strengths and weaknesses of these might be of interest. There are heavy bits and light bits, but it's mostly light.

SPIN

- *The intrinsic angular momentum of a subatomic particle*
- *To move, or cause to move, through the air with a revolving motion*
- *The presentation of information in a particular way; a slant, especially a favourable one.*
- *A brief trip for pleasure*
- *[A yarn] Tell a long, far-fetched story*

Opening spin: INTRODUCTION

Spin, *the intrinsic angular momentum of a subatomic particle,* is the phenomenon behind Magnetic Resonance Imaging [MRI]. It was my knowledge of physics that first led me into this field. However, after working for forty-seven years as a medical physicist I've experienced many more types of spin. The NHS is constantly subject to reorganisation, and whichever political party is in charge, information about it has a habit of being spun in a particular way, especially a favourable one.

Sadly, it's not only politicians and managers who adopt this tactic. Research findings can be subject to spin, generally with the aim of attracting financial support. Headlines like "New Breakthrough in Alzheimer's Disease", come as good news to us all, until we read the details of how mice have had their memories slightly preserved. Studies on mice have a habit of not working out when they are tried on humans.

The main aim of this diary, however, is to take a trip for pleasure. Going for a spin to explore the wonders of medical scanners and other medical devices, and the enormous benefits to mankind that have resulted from the work of the pioneers who developed them. There are many tales, not, I hope, far-fetched, but illustrative of the various achievements, and illustrated for ease of reading. A picture is worth a thousand words. A sub-plot is to reflect on the organisational systems and processes within the NHS and universities, and to look back on some of their strengths and weaknesses. And finally, there are a few gaps in the history of medical devices developed in Scotland. Perhaps tiny cracks rather than vast chasms, but maybe they should be filled in.

In the descriptions of the various devices there will be no mathematics, but you don't need that to understanding the basic principles. It all depends how you spin the story. Sadly 'spin' has come to be associated with deceit, particularly in a political setting. I don't intend to deceive, but simply to spin the explanations to focus on simple concepts. For those who want a more in-depth understanding of how some of the technologies work, plenty of on-line sites are available. For example, medical imaging is explained at http://sinapse-cpd.dcn.ed.ac.uk/. This site has ten modules explaining various imaging techniques. It is free to access and a Q&A section at the end of each module enables you to assess your understanding. It's very useful for those going for job interviews, those who want to keep up with their children, or those who are just curious.

So maybe sharing some of my experiences of healthcare technologies and public-sector management systems would be of interest. Or would it? Nobody gets murdered, although a fictional murder mystery inspired by NHS managers was a thought. I decided to avoid that in case it turned into non-fiction. There will be no drugs, sex, or rock and roll; no scandal, no intrigue and no romantic heroine clutching victory from the jaws of defeat. So, the reason for reading this will not be to second-guess how the plot will end. The reason has to be curiosity. How do these devices work? What are they used for? How were they developed? What is it like to work in medical research? Why does the NHS always struggle to meet performance targets?

Or, now that I've retired, do I have a secret about a senior civil servant that I can now reveal? So maybe there is intrigue!

Chapter 1: NUCLEAR SPIN

Wherever you go in a hospital or clinic you are likely to come across medical devices. Thinking about my impact on the development of these devices reminds me of Spike Milligan's "*Adolf Hitler: My Part in his Downfall* [2]. Spike wasn't central to the downfall, and I haven't been a leading developer of amazing breakthroughs in healthcare technologies. I've been one of many working in this setting, and like most of my colleagues, I gave it my best shot. That's all. A few special individuals make a big difference, but most of the progress in healthcare is down to the vast majority of workers who make small differences in specific areas of application. This is an account of some of my experiences in that setting. To understand why I chose this particular field of work a brief personal résumé might help to set the scene.

Doing what comes naturally

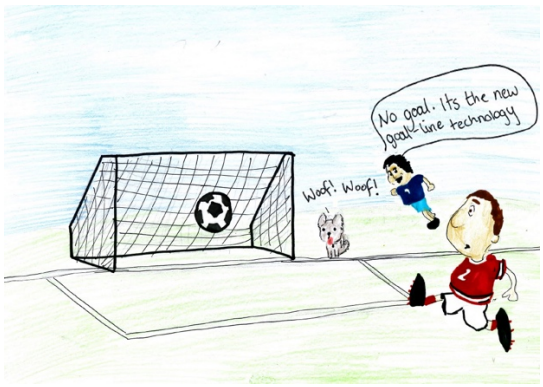
Folks are dumb where I come from
They ain't had any learnin'
Still they're happy as can be
Doin' what comes naturally…

Irving Berlin
from Annie Get Your Gun

The choices that we make at school quite often set us on a course for life. For me, it all started at Eastwood Senior Secondary School to the south of Glasgow. I don't think we were dumb, and we were certainly given plenty to learn. Perhaps we were fortunate to be in a generation that could drift through school and do what came naturally without too much thought being given to the career that lay ahead. Needless to say, Eastwood School has been subject to spin since I was there, both in its location and in its setting. It is now Eastwood High School.

This was before education professionals were strangled by curricula. When the topic of performance indicators comes up later, I suspect teachers might feel that those of us in the NHS are getting off lightly. We had excellent and enthusiastic teachers, and most of them would go the extra mile to help us. This was when my interest in science first started, perhaps due to rather eccentric teachers in physics and chemistry.

They wouldn't get away with their eccentricities today, but they knew their subjects and were certainly not dull. We had a wide range of extracurricular activities, so were happy as can be: striving to pass exams, witnessing explosions in the chemistry lab, going on rambles, the jazz club, the school concert, playing football with jerseys for goalposts – no VAR for us. There was loads to do.



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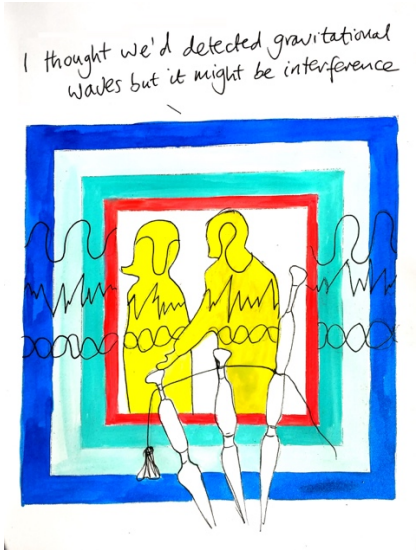
I ended up with a ridiculous number of passes on my higher leaving certificate due to spin. A decision was made to reorganise the higher leaving certificate examinations. In my fifth year I managed to pass the higher science exam. I then went on to do a sixth year and at that stage science was spun into separate disciplines, enabling me to get passes in physics, chemistry and biology. This was my first experience of four for the price of one.

The next move was to University.

Physics at the University of Glasgow

Physics was taught at most universities when I started in 1964, although at the University of Glasgow it was called Natural Philosophy. So, I'm really a philosopher. Physics is a very broad topic and understandably individual universities concentrated on topics that the lecturers knew about. At Glasgow we had a fascinating mixture of lecturers. For dynamics and mechanics our lecturer was Seamus MacNeill.

We enjoyed his lectures, but I don't think he did. He would far rather have been playing the bagpipes. Seamus was one of the founding members of the College of Piping in Glasgow, established in 1944. He had researched the physics of the great highland bagpipe, along with a fellow student, John Lenihan. John went on to set up the Department of Clinical Physics and there will be much more about him later. Often the distant tones of the *Lament for the Students* could be heard coming from the attic above the lecture room within minutes of the end of Seamus' lectures.



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The most charismatic lecturer was Ron Drever, who lectured on solid-state physics. Ron was always bursting with energy and enthusiasm. He was slightly round in shape, and he used to amaze us by producing several valves and pentodes from his inside jacket pocket. He produced these quite large objects, but he didn't appear to change shape – and we had expected quite a large change in shape. It was a strange physical phenomenon. Ron went on to pioneer the detection of one of the smallest changes in shape known to man - the changes in the shape of the world around us due to gravitational waves. He was one of the three researchers who devised the Laser Interferometer Gravitational-Wave Observatory LIGO. His research had already started when we were his students and in 1970, shortly after I left, he created a group at Glasgow University focusing on gravitational wave detection. On September 14th 2015, forty-five years later, for the first time, the ripples in space-time reaching earth from a black hole collision in a distant galaxy were detected. Ron wasn't one of the many who made a small difference. His impact was massive. Janna Levin has written a fascinating account of the discovery of gravitational waves in *Black Holes and other Songs from Outer Space* [3]. In this book Ron is described as being both brilliantly innovative but also an awkward character who resisted collaboration. We experienced the bright side.

It was Professor John Gunn's lectures on atomic and nuclear physics, however, that first introduced me to spin. The nucleus of an atom has a property called nuclear spin. This is an interesting phenomenon. It helps to explain how magnetic resonance imaging [MRI] works. We were taught that nuclear spin is a natural phenomenon that can be explained by classical physics as a type of angular momentum, a very small-scale version of a spinning top, or by quantum physic as discrete energy states that could have numbers put on them such as +1/2 or -1/2. For ages I grappled with the duality of these explanations, but I shouldn't have. We think of physics as 'absolute truth', but what does that mean? Is there such a thing? The human race has developed a desire to understand things, and in order to quench our thirst for explanations we make up stories. To help to make sense of these stories physicists use mathematics to sort out the thought processes. This is enormously useful as it can bring aspects of the story together and make predictions about how the story might go from here. The stories that I'm referring to are often called scientific theories, but they are really just stories that

help to clarify our thoughts. If there is more than one way to tell the story, why should we be surprised?

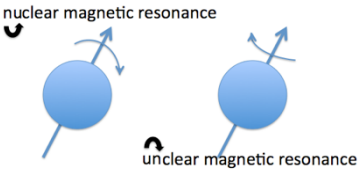
Currently theories in physics are incomplete. There is no grand unifying theory that can explain all observations. Perhaps the limitation is the human brain, and the extent to which it has evolved. Would a more developed brain help? What about artificial intelligence? Will computers help to sort this out? I wouldn't bet on it.

So, over time, most scientific theories are either replaced or modified, but that doesn't prevent them from being useful. Without them there would be no MRI and medicine would be much the poorer. On top of this, the theories that we develop about how the brain works are informed by MRI and by measurements made using other scientific devices, themselves devised with the aid of theories. So, this is a really helpful process and I certainly don't want to downplay the importance of scientific theories for creative thinking and technology development, but 'absolute' truth? Maybe in our minds only? Note that I've emphasized 'absolute' as clearly there is such a thing as truth. In the presidential election in 2016 only 46.2% of US votes went to Donald Trump – truth. Arsenal beat Chelsea 2:1 on 27th May 2017 – truth. Both of these can be backed up by factual evidence. The nucleus of an atom has a property called spin – story. It's a good story as it fits with loads of observations, but it's still a story.

What is important about the nuclear spin stories, or theories, is that they help us to describe how nuclei can absorb radiofrequency energy as long as this energy is at the appropriate frequency for particular atoms in the body. This process is called resonance. A commonly used analogy is the absorption of sound waves by a tuning fork, or the shattering of a glass by an opera singer. These are, of course, analogies, as sound-waves are not quite the same as the radio-waves in MRI. Sound waves oscillate forwards and backwards whereas radio-waves, and all the different types of waves in what is called the electromagnetic spectrum, oscillate across the way, at right angles to the direction of travel.

An MRI scanner is really a form of radio transmitter and receiver. Before being used as a technique to scan the body, nuclear magnetic resonance devices were used in laboratories to identify specific substances by the signatures of the frequency of oscillations in their nuclei. When it was realized that a variation in this process could be used to scan internal organs in the body the scanners were initially called nuclear magnetic resonance scanners. However, the association with other devices with the label of 'nuclear' was felt to be potentially alarming for patients and so 'nuclear' was dropped from the title.

So, MRI can be described using quantum physics and energy levels or by classical physics with diagrams of spinning tops and magnetic fields. Mathematical equation can be produced to describe the observations and to help to make predictions - for example, how the timing of signal detection might alter the contrast between the signals from fat or from bone. The theories and mathematical explanations can be traced back to the pioneering work of Scottish Physicist James Clark Maxwell [4] 150 years ago. On the centenary of Maxwell's birth, Einstein described his work as the "*most profound and the most fruitful that physics has experienced since the time of Newton*".



Some explanations are clearer than others

Maxwell developed the classical theory, with spinning top analogies, but some aspects of MRI are easier to describe using quantum theory. You can pick and choose. MRI will be described in more detail later.

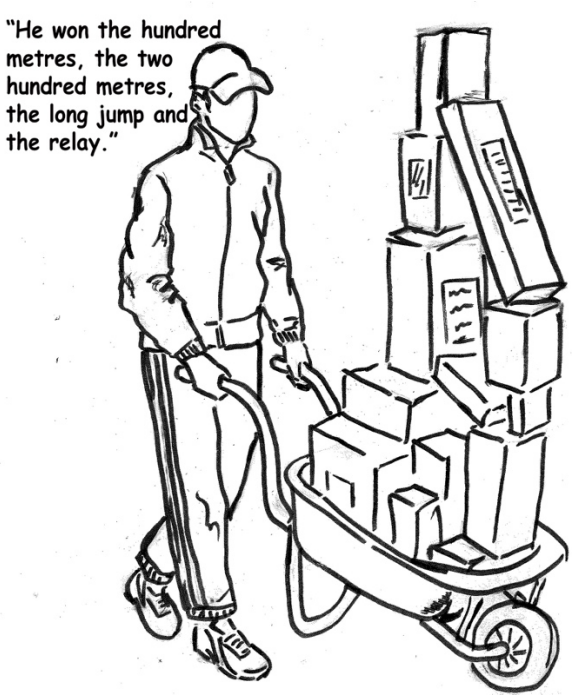
Towards the end of our physics degree course we had to start thinking about where we would go next. The focus turned to job interviews.

Job Interviews

I suppose there's a fair amount of spin in the interview process. You have to review your skill-set and spin it until the profile becomes a best fit for the job in question.

I remember two interviews in particular. One was with Imperial Chemical Industries (ICI) at Billingham in the north of England and the other was at the Medical Physics Department of the West of Scotland Health Board.

I headed down to ICI, not really knowing what to expect. The recruitment process involved a formal interview followed by lunch. In my naivety I didn't realise that the chat over lunch was the more important of the two events. There were three interviewees and three hosts. They were probing our outside interests and, as one of mine was athletics, the topic of amateurism in sport came up. Those were the days when professional sport was just beginning to appear and so this was a hot topic. Central to the debate was the issue that if monetary rewards were to become too large, then the incentive to cheat would be increased. I liked the notion of amateur sport, although I suppose we did end up winning far too many canteens of cutlery as we went round the circuit of Highland Games athletics events. I was batting strongly for the amateurs when it dawned on me that I was going head to head with one of the 'hosts'. I promptly shut up, but when I looked him in the eye, he gave me a smile, suggesting that maybe he had quite enjoyed the encounter. They did offer me a job.



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The second interview was at the Medical Physics Department in Glasgow. At that time, 1967, no hospital in the country had a CT scanner, or MRI or PET. Physicists and engineers were still developing them in universities and factories. However, technology was starting to become important in healthcare and so Medical Physics Departments were expanding rapidly. The interview process didn't include lunch and maybe it should have, but they too offered me a job. So, I had a major life decision to make. It was really a very easy decision. The salaries were almost identical at around £1000 a year, but the Medical Physics Department offered the option of studying part-time for a PhD. The 47-year stint had begun.

Medical Physics: The learning curve.

The first of my seven posts in medical physics was, not surprisingly, as a trainee. This was perhaps the steepest learning curve in my whole career. I knew quite a lot about physics, but nothing about physiology, pathology or medicine. One feature that distinguished my learning curve from what is now in place is that at the time no formal training programme had been set up. I was employed by the Health Board, enrolled as a part-time external doctoral student at the University of Glasgow, and spent five years combining routine work in medical physics with research for my PhD. However, there was no teaching component in the PhD. I learned by being there, doing work, asking questions and experiencing the thought processes of colleagues.

Now our professional body, the Institute for Physics and Engineering in Medicine [IPEM], has a comprehensive and quite tough formal training programme with external assessment. Not for one minute would I advocate rolling back the clock to my experience of just learning on the job, but having to take ownership of our need for knowledge and having to go out and forage for information is a skill that stood us in good stead throughout our careers. I don't think that it would be appropriate

for medical physics today, but 40 years ago we were less specialised. New technologies were rapidly finding uses in healthcare and so regularly we had to learn completely new skills.

Certainly, one feature of our experience of learning on the job was that it was thoroughly enjoyable. We weren't swotting for an exam, but were exploring an exciting new world. How does this scanner work? How are these electrical signals from the body amplified? How are they generated in the first place? Why do some patients deteriorate after a head injury and others don't? What treatments are available for Parkinson's Disease? How do they work? It was an endless list. You would sit up late into the night because you didn't want to go to work the next day not knowing the answers. In those days we couldn't get information and mis-information from the internet, so we had to get both of these from textbooks, scientific papers and colleagues – both fellow medical physicists and other professionals, mainly clinicians. We learned the job because we couldn't function effectively if we didn't, but we didn't have a certificate to show that we'd passed exams, and you do need that. It's not good enough for you to know in your own mind that you are competent. Employers need evidence.

Studying for a PhD: Doctor of Philosophy

As one attraction of the job was that it came with the option of studying part-time for a PhD, I felt obliged to take up the offer. Compared to the alternative of registering with a university for a full-time studentship, this had the disadvantage of taking five rather than three years and having to be done largely in what was called our 'own time'. However, that had to be offset against that fact that we were also training for our profession and had a clear career-path in sight. I can't say that I found the experience stressful, although I've met several colleagues who have. I was very fortunate. My supervisor was Dr Frank Gillespie, who had a brilliant mind and was kind and understanding. A good supervisor makes all the difference.

The objective of my PhD was to improve the clarity of images of high-energy gamma rays coming from the body. At the time, around 1970, medical scanning was a relatively new innovation. The type of scanner that I was working on was called a rectilinear scanner, designed to build up a map of the distribution of radioactive materials called tracers that had been administered to patients. The tracers have two distinct features. They contain chemical compounds that have biological properties, such a sticking to particular types of cells, and they emit gamma radiation. They contain tiny amounts of the chemical substances, because larger amounts would alter what we are trying to measure. Also, they emit tiny amounts of gamma radiation to limit the likelihood of radiation damage. That means that the detection process had to be as efficient as possible.

To get the positional information on the distribution of the tracer, the scanners need a way of detecting only those gamma-rays coming from a small region in the body. These rays don't bend like light and so can't be focused by a lens. Instead, the gamma-ray detectors need what are called collimators, which are blocks of lead with specially shaped holes. The rays passing through the holes can be called the signal, because we want to detect them. Gamma rays coming from other regions should be blocked out by hitting the lead. If they get through the lead they are the noise. The collimators have to maximize the ratio of signal to noise. The energy of the gamma-rays is an important consideration as higher energy rays can penetrate the edges of the lead.

After modeling various designs, we came up with one that would give the best focus for the high-energy gamma rays that were in use in medicine and we had a collimator built to the new specification. Geronimo! It worked. The focus of the scanner was improved. I wrote a paper for one of the Medical Science Journals, Physics in Medicine and Biology, and waited for the plaudits. A letter from the journal arrived a few weeks later. 'Rejected'! I couldn't believe it. The problem was that I had adding extra bits on to the ends of the collimator, making it longer, and so the detector was further away from the source and the overall signal weaker. Fewer gamma rays were detected. So, the focus was better, but at the cost of lower detection sensitivity. *But, 'rejected'! The reviewers are idiots. Of course this is a better design. Are they daft?*

No. They were right. With my tail between my legs I went back to the drawing board, redesigned the collimator to be the same length as the original but incorporating tapered holes, recalculated the distribution profile, but this time also including the detection sensitivity, and then had a 'same length' collimator made and tested. It worked. We submitted another paper. It was accepted for publication

[5], and formed the core of my PhD thesis. Although I didn't think this at the time, having my first paper rejected was probably the best thing that could have happened. It taught me to question myself more, it gave me respect for those providing critical feedback, and above all it introduced me to the process that is central to science – peer review.

So, for the second time I was a philosopher. Having graduated initially in natural philosophy I had gone on to become a doctor of philosophy. Both, however, were really physics rather than philosophy.

There was a sting in the tale at the end of my PhD project. We had developed an improved design of collimator. Why didn't we patent this, or at least protect the design, sell out to an equipment manufacturer and wait for the money to roll in? In reality this seldom happens. The problem is that nothing takes place in isolation. The advantage of my design was that scanners would have sharper images for those tracers that emitted high-energy gamma rays. While all this was going on, a new material was appearing on the market – technetium-99m. It emits low-energy gamma rays. At first sight technetium was not the ideal gamma-emitting molecule to use for studies of human pathologies. It is not an element that appears in the body. However, chemists are a resilient bunch, and they were able to incorporate it into a whole range of materials that did have biological properties and could be used as tracers in medicine. So, we ended up using low-energy technetium compounds almost exclusively and higher energy gamma-ray emitters rapidly fell out of favour. My collimators improved the clarity of images of high-energy gamma rays just as their use in medical imaging was drawing to a close. Most technological innovations have a time window, but some are shorter than others!

We're now heading for a physicsy section, but don't be too phased. It's light. Not light as in *visible electromagnetic radiation*, or *set fire to*, or *a pale shade of colour*, but light as in *not profound* and hopefully *enlightening*. Medical imaging experts will be able to gloss over it quickly.

X-ray Detector Spin. COMPUTED TOMOGRAPHY – CT

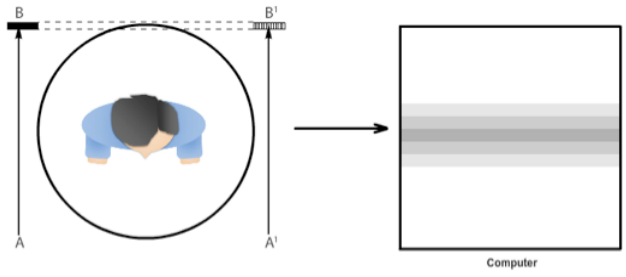
In 1972 Godfrey Hounsfield produced the first commercial CT scanner, called the EMI-scanner, while working at the laboratories of EMI in Middlesex. I often delighted in slipping a quiz question into my lectures to students about the physics of the CT scanner. *Name four people who helped Godfrey Hounsfield to develop the first CT scanner?* Answer: *The Beatles*. It was at a time when the coffers of EMI were being swollen considerably by sales of records by the fab four. Having read the excellent account of Hounsfield's developments by Stephen Bates *et al* [6] it is quite clear that I was presenting a misleading picture. Like many great innovators, Hounsfield had to scrape money together. The main contribution from EMI was that they let him get on with it.

He also wasn't helped much by radiologists. He went to various hospitals and medical schools to see what they thought of the idea. It was very discouraging. The experienced radiologists were so steeped in the clarity of their X-ray pictures that they couldn't see the advantages of a technique that would produce less clear images. They couldn't appreciate the benefit of seeing much more, as organs would be defined in three dimensions, and they were ignoring the enormous benefit offered to those imaging the brain – the ability to image inside the skull. However, the opinions of the masses can often be overshadowed by support from an influential and respected enthusiast. This came from Dr James Ambrose, a consultant radiologist at the Atkinson Morley's Hospital in south London. It was Ambrose who provided clinical support and created history by conducting the first CT scan on a living patient.

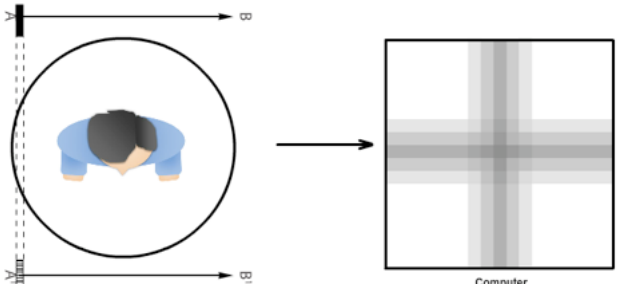
Illustrations to explain the working of CT scanners.

Computed Tomography has two elements. 'Tomography' is straightforward. It means looking at sections through the body. What a pathologist would see with a slicer. It's the 'Computed' part that is harder to grasp. Whereas a plain X-ray used photographic film, CT needs numbers and computers. To do this the X-ray detectors have to convert the intensity of the X-ray beam into numbers that can be fed into a computer. This needs an electronic gadget called an analogue to digital converter. The X-ray detectors are not photographic film, as with the original medical X-rays, but devices that generate an electric voltage. The higher the voltage, the bigger the number that is fed into the computer. Thereafter, the maths can get complicated but the principle is straightforward.

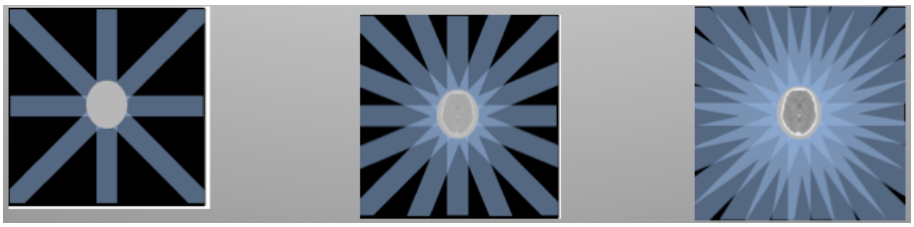
If we have an X-ray source at position B on the left and a detector at position B' on the right, and if we move this assembly from bottom to top, the numbers fed into the computer will be smaller as the assembly passes the head, because the head will absorb some of the X-rays. This is shown as darker on the diagram.



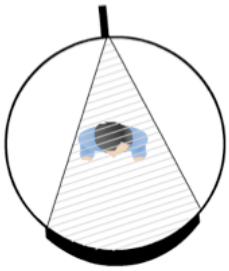
Now repeat the process with the assembly rotated through 90 degrees and add the two sets of numbers together. Already it is becoming possible by looking at the image on the right to determine that the head is in the middle of the picture.



Now repeat the process at more angles and the detail starts to improve still further until the structures inside the body start to become clear. This process is called back-projection.



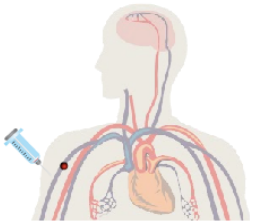
The next stage is to move the detector assembly slightly to scan another slice. In this way three dimentional images can be built up. A plain X-ray is two dimentional and so lacks any information about depth. CT provides this. The basic principle is simply to look from several angles. It's like life in general. If you just look at an issue from one angle your information can be grossly distorted. The more angles you look from, the more informed you become.

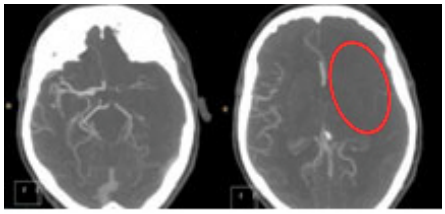


The X-ray tube and detectors spin back and forth, a bit like the drum in a washing machine.

With the original EMI scanner it took an hour for the detector assembly to scan the head and a further hour for the computer to do the maths. Today's CT scanners have seen many advances in design and in computing power. A fan beam of x-rays with one source and banks of up to 256 individual detectors has replaced the linear assembly and a scan of the body takes only a few minutes. The forty-five years since CT was developed have seen healthy commercial battles to develop scanners with go-faster stripes and the production of improved images with lower intensity X-rays beams, but the basic principles remain the same.

CT angiography Often radiologists are more interested in looking at blood vessels than at organs in the body. Blood vessels are crucial. All tissues require oxygen and oxygen is delivered by blood. Blood vessels can block or they can burst. Either is bad news. The technique to enable CT scanning to study blood vessels is simple. A dense material, called contrast, because it provides an additional contrast in the images, is injected into a vein and then travels throughout the bloodstream.





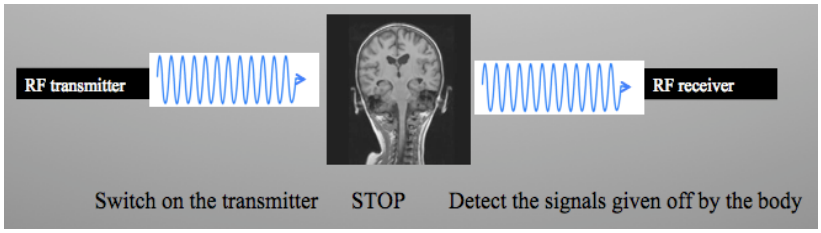
The dense material is typically a compound containing iodine, which has a high absorption of X-rays. You can see the blood vessels in the images above. These CT scans were taken from a patient who has had a stroke, which blocked some of the vessels in the right-hand side of the brain.

Nuclear spin: MAGNETIC RESONANCE IMAGING - MRI

I've already discussed the 'spin' aspect of MRI. Spin is the phenomenon that enables radiofrequency [RF] waves to be absorbed and then emitted by tissue as long as the tissue is in a magnetic field and the frequency of the RF is such that resonance can take place. I should emphasise again that this is not intended as a detailed educational guide. A complete explanation of the workings of MRI would fill several books, and there is no need to do that here as many teaching books and websites are available. However, to save looking these up, there are a few aspects that can be explained simply. The most fundamental issue is to illustrate how magnetic resonance can be used for imaging.

Magnetic Resonance Imaging and some of its derivatives

The signal comes from RF energy that is absorbed by the body and is then emitted.



If you walk into a warm room, you heat up. Then when you go to a colder setting you radiate heat and cool down. First you absorb energy and then you give it out. This is similar to the absorption and emission of RF energy, but absorption happens only if the RF beam is at just the right frequency for the magnetic field strength of the MRI magnet. A more familiar example is the signal picked up by a tuning fork. If you slide your finger up the string of a fiddle, you'll find a point at which the tuning fork starts to vibrate. This happened when the frequency of the sound waves is the same as the frequency at which the fork vibrates most easily. This is resonance.

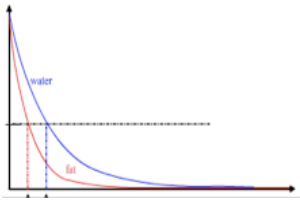
However, how do we know precisely where in the body the signals are coming from? Every imaging technique needs two basic components – contrast to distinguish one type of tissue from another and positional information.

Positional information comes from applying small variations to the magnetic field, called **magnetic field gradients**. They can be applied while the RF energy is being absorbed by the body when RF is beamed in from a transmitter, and also to the detection of RF emitted from the body later on.

As you look along the green line, if the magnetic field is slightly stronger at the head end of the scanner than at the other end then the resonance frequency will increase slightly from bottom to top. There will be only one thin slice somewhere along the green line where the frequency is just right, and the RF energy will be absorbed.

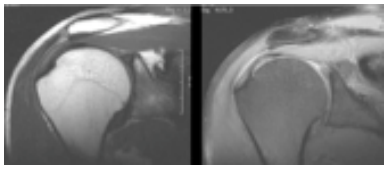
So, by applying the magnetic field gradient when the RF energy is fed in we can restrict the absorption to one slice. We apply similar gradients while reading the emitted signals and this can be done at various times and in various directions, giving three-dimensional information. So positional information comes from small alterations to the magnetic field strength - magnetic field gradients.

Contrast in the images comes from the basic fact that different tissues lose energy at different rates. Fat [in red] loses nuclear spin energy faster than water [in blue], so if a measurement is made a few milliseconds after the RF transmitter is switched off then there will be a higher signal coming from watery tissue than fatty tissue.



Movement of tissue also affects the rate of loss of the spin signal. We'll come to that later

In practice, the designers of MRI scanners can be very imaginative and can play around with the timing of when energy is fed in and when it is measured. They develop what are referred to as pulse sequences. They can alter the timing of when gradients are switched on and off, and when RF is beamed in or measured, and in doing so can radically alter the contrast in scans.

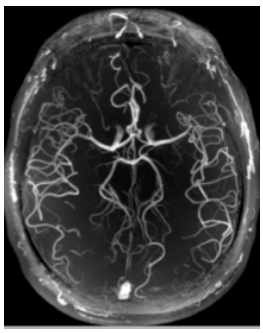


These scans of a shoulder joint show that the contrast can be changed just by using different pulse sequences. It the same shoulder, scanned with different pulse sequences

This is one of the big advantages that MRI has over CT, where the contrast can't be altered so much. When a patient is referred for MRI the first question the radiologist will ask is "What are you looking for?" Only by knowing this can the pulse sequence that will give the best contrast be selected.

We have already looked at how CT can be used to study blood vessels. The same can be done with MRI, but instead of injecting into the blood stream a material that absorbs X-rays, we can inject a material that alters the rate at which nuclear spin signal is lost. Typically, this might be a compound containing the metal gadolinium, which is referred to as being paramagnetic, and so alters the rate of loss of nuclear spin energy and so produces contrast in the images. However, with MRI there are other techniques that enable blood flow to be measured without injecting anything into the body. There are several ways of doing this. One of these is called arterial spin labeling. If the RF signal is absorbed at one slice through the body and then a short time later the emitted RF signals are measured at a different slice, then blood that has moved from the first slice to the second can be identified by comparing two scans, one with an RF signal applied in the first slice and one without. The movement of blood is detected by feeding the energy in at one slice and detecting it at another.

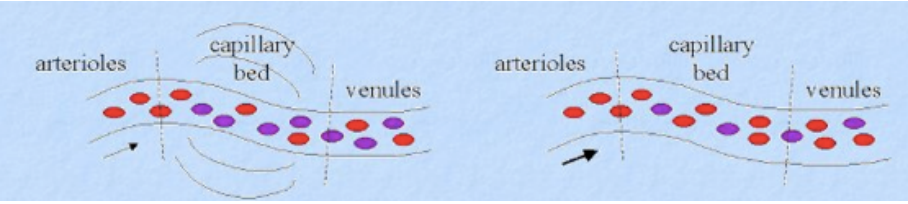
Very high definition images can be obtained, such as this one from a 7Tesla MRI at the Queen Elizabeth University Hospital in Glasgow.
Image courtesy Professor Keith Muir.



Most MRI scanners have a magnetic field strength of 3 Tesla. By increasing this to 7 Tesla better image definition can be obtained. The clinical benefits of this are currently being explored.

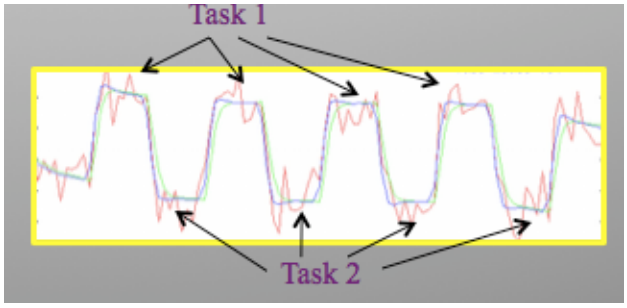
I mentioned that gadolinium is paramagnetic. Another paramagnetic material is oxygen, and this has led to the widely used technique of functional MRI [fMRI]. I'll not describe this in full, but the basic principle is straightforward. We've already seen that any image needs a contrast between the characteristics of one part of tissue with another. In CT the contrast comes from different tissues absorbing different amounts of X-rays. X-ray absorption depends on the density of electrons in the atoms making up the material, and this is what characterises the material. In MRI it is the change in nuclear spin signal that characterizes the material. However, the nature of MRI means that there are many tricks waiting to be exploited. One of these is to make use of oxygen. Oxygen is paramagnetic, which means that it causes the nuclear spin energy to be lost more quickly. The more oxygen the quicker the loss of signal. Now nature steps in.

When we use our brains, which is all the time, some parts work harder than others depending on what we are doing. If we are looking at something, then the part of the brain at the back called the visual cortex is being used. In order to function it uses oxygen. The body is designed to respond to this and so blood vessels carrying the blood expand in order to deliver more oxygen. However, as with many other processes in nature, the initial reaction is an over-compensation, and so an excess of oxygen builds up in this region for a short time. The illustration shows that there are more oxygenated blood cells in the small veins [venules] just after the task has been performed.

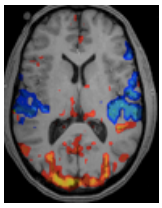


Blood cells with oxygen are shown in red and those without in purple. The small veins have an excess of oxygen in regions that have done more work. So, if two MRI scans of the same region are done when the task is being performed and then when it isn't, a contrast can be obtained. The MRI pulse sequence that is used is one that is sensitive to the amount of oxygen and is called the BOLD sequence – Blood Oxygen Level Dependent. MRI experts love acronyms.

The result is an image showing the difference in oxygen levels between task one and task two in each part of the brain. Task two can be resting, so just letting your mind wander, but this can be a bit uncontrolled and so often two different states of activation are compared.



Here task 1 involves vision and task two is with eyes closed.



The yellow and red bits are the visual cortex. The blue bits show regions with lower brain activity during this task.

This can be illustrated using a study that we set up for John, one of the PhD students. It produced results that were of sufficient interest to be published in a reasonably prestigious journal [7]. There had been considerable interest in using this technique to study depression, but we chose to explore the other end of the mood spectrum and look at elation. How does the brain respond to moments of extreme happiness? A few studies had been done elsewhere. Chocolate was one of the favourite sources of pleasure, and, of course, sex, but the Scandinavians had covered that and there's no way that we would get moral approval, far less ethical approval, in central Scotland for such a study. Instead we chose a passion that at the time could bring fleeting moments of extreme please to a certain section of the community – football supporters. We reckoned that the study would work only if the participants were passionate about the game and so a group of holders of season tickets for the local football team in Govan were selected.

The willing volunteers had to lie in the MRI scanner and watch video footage of previous games. The images were then analysed by comparing three stages: 1) what is called 'open play' – when the ball is being aimlessly kicked around near the middle of the pitch; 2) goalmouth activity when there is a chance that a goal might be scored and so **anticipation** sets in; and 3) a goal being scored. The contrast between a goal being scored or missed enabled us to distinguish between extreme **pleasure** and disappointment. We were able to find regions of the brain that were activated during the anticipation phase and others that were activated by extreme pleasure, and the findings were consistent with other studies. One of the pleasure centres is called the anterior cingulate, a region in the mid-frontal part of the brain. I'm not aware of this finding having been replicated with other sports but I'm sure that it could be. There has been one other study that used soccer as an emotional stimulus. This was by a German group who compared the effects of soccer to those of monetary reward. They also found involvement of the anterior cingulate cortex [8].

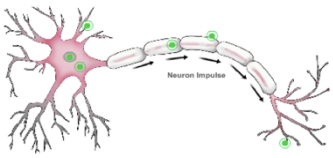
These findings didn't come as a complete surprise because there is another way of investigating which parts of the brain are involved in specific tasks and emotions. Patients who have damaged or malformed parts of the brain, often experience specific deficits and knowledge of the site of the damage can tell us about the role of that specific part of the brain. People with damage in the anterior cingulate can experience mood problems, and this points to a link between this region of the brain

and mood states. Patients with clinical depression can be treated with drugs that affect the overall chemistry of the brain, but there are also two additional options that target the anterior cingulate region specifically. They involve completely opposite approaches. The anterior cingulate can be stimulated using electromagnetic radiation or it can be disabled by a process called ACING [Anterior CINGulotomy], which involves burning part of it out [9]. This might appear contradictory, but both processes have been shown to be effective in well-selected patients. In some cases, it might help to give that part of the brain a kick-start to stimulate activity, whereas in others it might be functioning in the wrong way and it's better to remove it. A very effective use of tissue removal can be found in epilepsy. In patients whose epilepsy involves the part of the brain called the temporal lobe, it has been shown that symptoms can be radically reduced by taking this part of the brain away. It's called temporal lobectomy. This process clearly requires detailed brain scanning and electrical recording prior to surgery to identify the faulty part of the brain. Unlike taking drugs, the treatment can't be reversed!

Mapping the highways with MRI

Recently MRI has been taken a stage further. Again, this technique exploits the fact that movement speeds up the rate of loss of the nuclear spin signal. Albert Einstein published an article in 1905 about what is called Brownian motion [10]. This is the random motion of particles that are suspended in a fluid. MRI is able to map connecting pathways in the brain by detecting restrictions to this movement.

On the right is a diagram of a connecting nerve fibre in the brain and on the left is a simplified drawing depicting the constraint of movement.



The size of the RF signal that is detected in an MRI scanner is affected by movement and so magnetic field gradients can be used to detect the amount of movement in different directions.

The result is that stunning images like the one shown here can be obtained.

The different colours represent nerve pathways with different alignment. We are not scanning individual nerve fibres. The image here shows bundles of fibres in the white matter of a brain.

This is like a road map. It shows the routes, but not how busy they are. Its use is particularly exciting in brain conditions that appear to be associated with signaling pathways. So, in psychosis basic MRI might not show any structural abnormality, but this new technique is being used in research to explore possible abnormalities in the bundles of white matter fibres that send signals around the brain.

The clinical value of MRI and CT

The MRI scanner that I first worked on was installed in 1984, well before the techniques of functional MRI or diffusion MRI had been developed. This was the first commercial scanner to be installed in Scotland, although researchers in Aberdeen working in the team of Professor John Mallard had the fun of building their own. I'll discuss John's work later. One of our objectives was to evaluate whether MRI was better than CT in certain clinical settings, in particular in the management of head injured patients. This is important. Radiologists, understandably, like devices that produce images of higher quality. MRI images, even at the relatively low magnetic field strength of 0.15Tesla that was used in those days, clearly produced better images than CT. The question was, 'does this matter?' Does it

improve the management of patients? Do you detect details that are missed on CT, and are they important details?

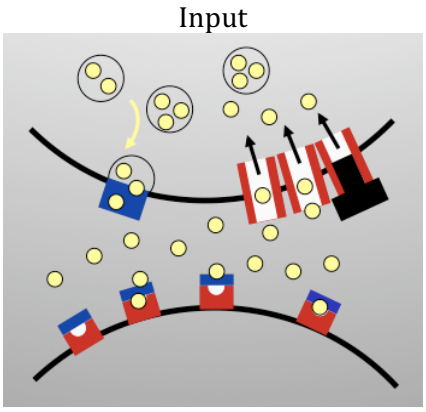
The answer was that MRI was better, picking up twice as many abnormalities as CT and significantly altering patient management [11]. Over the years both technologies have improved. The gap between MRI and CT has widened, but there is still a place for CT. It is fast and can be used in settings where MRI can't, such as on patients with ferromagnetic objects in their bodies [shipyard welders being a good example] or patients who suffer from claustrophobia. If a patient with an acute stroke is admitted to hospital speed is of the essence. 'Time is brain' is the slogan. Every minute after a stroke starts 1.9 million brain cells are lost and every nine minutes the disability increases by 1%. A stroke can be caused by a blood clot or by a bleed from a blood vessel. It is vital to know which type of stroke a patient has, and a quick CT scan can give the required information. In fact, what is really required is to have a CT scanner in the ambulance that collects the patient. Recently Samsung Neurologica brought out a stroke ambulance with CT on board. This might well be the future.

Positron Emission Tomography: PET

We have seen that CT contrast depends on the density of tissue in the body and that MRI contrast depends on the nature of that tissue – whether cells are tightly bound or free to move around a bit. MRI can be developed to identify regions that are selectively involved in the performance of tasks and it can map connecting tissue. However, neither CT nor MRI can study individual molecular processes. A brief look into the functioning of the brain can help to explain the need for this.

The brain communicates with itself and with other parts of the body by sending electrical impulses along nerve pathways. This process is controlled by what are called synapses. These are chemical gates.

In this very simplified illustration of a synapse, the electrical signal comes in at the top, causing a chemical substance called a neurotransmitter (in yellow) to be released into the middle of the synapse where it can be attached to molecules on the output called **receptors** (blue and red with a hole at the centre). This alters the output electrical signals. To prevent too much neurotransmitter building up in the middle, molecules on the surface at the input end (red and white) help to absorb some of it back in. They are called **transporters**.



Receptors and transporters are molecules that control the electrical signaling in the brain. The concentration of these molecules has a profound effect on activities and emotions. There are many types of synapse, characterised by the materials that they contain. Dopamine synapses influence movement, and they are defective in Parkinson's Disease. Serotonin synapses influence mood. One treatment for clinical depression is to use drugs called selective serotonin reuptake inhibitors – SSRIs. They reduce the reuptake action of transporters and so leave more serotonin in the synapse in the hope that this will improve the patient's mood.

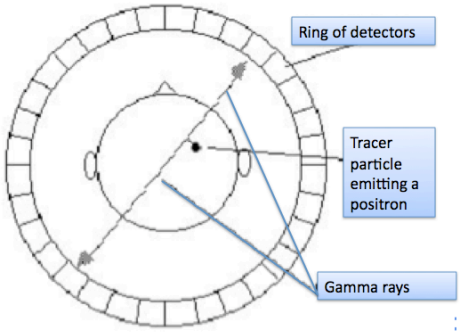
How can we measure the amount of these chemical substances? The trick is to use other chemicals that attach to the ones we want to measure. If these other chemicals send out a signal that can be detected outside the body, then we have an imaging technique. We could use substances that would alter the rate of loss of nuclear spin energy and so provide a contrast for MRI, but in practice the signal would be far too weak. Instead we use chemicals that give out gamma rays. They can be detected by very sensitive gamma ray detectors and give enough of a signal to enable good images to be produced. The first stage in the process is to prepare the chemical that emits the gamma rays. It is called a radio-pharmaceutical – radio because it gives out radioactive gamma-rays that penetrate through the body, and pharmaceutical because it behaves like a drug. For simplicity they are called tracers, because they enable us to trace the amounts of specific molecules in the body. Tracers are radioactive and are also drugs. That sounds a bit scary. It isn't. The amount of radioactivity is extremely small. The radiation dose to the patient is very tightly regulated. Also, the amount of drug is extremely small. Otherwise it could affect the process that is being investigated. The tracer is injected into the body, usually into a vein in the wrist. It then travels around the body and is taken up by organs such as the brain or the heart. These organs are then scanned.

Positron Emission Tomography scanners

The term emission tomography is used because the signal comes from gamma rays that are emitted from the body after administering the tracer to the patient. There are two types of scanning process, depending on the type of gamma-ray emission. The simpler technique is called SPECT – Single Photon Emission Computed Tomography. A photon is a gamma ray, so this is really similar to X-ray CT, but the photon is emitted from the body rather than coming from outside and passing through the body. To build up a series of images a gamma camera is used. This is an instrument with a gamma ray

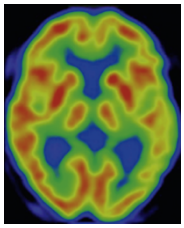
detector to pick up the signal and a collimator to determine where it came from, somewhat similar to the ones in my PhD thesis.

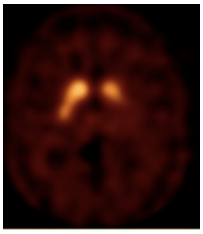
The alternative scanning process is called PET – positron emission tomography. The radioactive materials in PET give out positrons rather than gamma rays. Positrons don't travel far before they hit an electron. That's the end of the positron as it is converted into two gamma rays.



The bonus is that these two gamma rays are given out at 180 degrees to each other. This means that their position in the body can be calculated without having to use collimators, which is bad news for collimator designers, but good for detector efficiency and hence quality of image. We have seen that in CT as long as you have data from enough angles you can use back-projection to build up an image. With PET, if two gamma rays are detected at each end of the line at the same point in time then you know they originated somewhere along the line joining the two detectors. This is called a coincidence event. If all the co-incidence lines are back-projected the locations where they originated will start to appear – just as in CT.

Here you can see a PET scan of the brain. The tracer used was FluoroDeoxyGlucose – FDG, which behaves like glucose, the body's source of energy. The red bits in the image are grey matter. Brain cells that use a lot of glucose. Scans like this can be helpful in the diagnosis of dementia as they detect which parts of the brain are affected, and in cancer, to identify regions with excess glucose use.



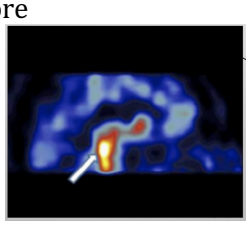


These scans are of the same parts of the brain as the ones above, but a different tracer has been used; one that helps us to study the **dopamine** neurotransmitter system, which has been shown to be particularly associated with feelings of reward and with motor control. It is affected in Parkinson's Disease and these scans help in the diagnosis of PD.

The scans are of a horizontal slice at the mid-level of the brain. The one on the left is normal but the one on the right has a low signal from the regions that look like tails of inverted commas. Although the symptoms were fairly mild, the scan confirmed that the patient has PD.

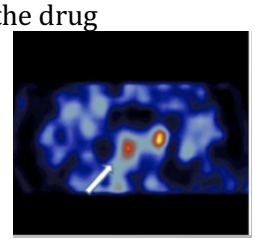
One of the most exciting uses of PET is in the **study of drug action.**

Before



Images courtesy of Dr Sally Pimlott

On the drug



These are scans of a patient before taking an antidepressant drug (left) and then while on the drug (right). The image in the middle is an illustration of the part of the brain where the tracer builds up. The particular tracer used here attaches to **serotonin** transporters. This is where the drug acts in order to reduce the reuptake of serotonin and so improve mood. If the drug has already attached to a

transporter molecule then the tracer can't. The site is already occupied. So, the bigger the difference between the scans *before taking the drug* and *on the drug*, the higher the drug uptake. Drug uptake levels can be quantified, and this is invaluable. Otherwise doctors would just know how much drug they had given, and not how much is being taken up at the site of action.

Why is this not done with every new drug that is brought to the market, and even older ones where the uptake has not been studied in relation to clinical effectiveness? One answer is cost, but that's not a good answer. These studies have just to be done a few times for each drug. Perhaps the main reason is that producing an appropriate tracer for the scans is just as difficult as producing a drug. It takes a long time, and drug companies don't like to hang around.

The main clinical use of PET is in cancer diagnosis. The tracer used is usually FDG, because cancer cells use up more glucose than normal ones. However, tracers are at last appearing that can measure much more specific processes in tumours, such as whether or not they are short of oxygen or how rapidly they are reproducing. Studies are now underway to determine whether or not these new tracers improve patient management and are cost effective. So, the cycle continues. This takes a long time, but it's good science.

Radiation safety

PET has far more sensitivity than MRI for the measurement of specific molecular processes in the body, and yet medical imaging scientists are constantly trying to bridge the gap in sensitivity so that MRI could be used in some cases rather than PET. Why? Why not just leave it to PET? One reason is that PET is usually more expensive as it requires tracers that are rapidly losing their radioactivity and so have to be made at a site within a few hours from the hospital where the scanner is located. However, perhaps the main reason is that the positrons and gamma rays in PET are ionising forms of radiation whereas MRI uses radio-waves, which are not ionising. CT also uses ionising X-rays. If the radiation is ionising then it can alter DNA and if the immune system doesn't repair the damage then cancerous cells might develop.

We know that very large amounts of ionising radiation are damaging, but with the amounts that are used in medical scans we simply don't know if there is a harmful effect. In fact, there is a theory called radiation hormesis, which postulates that small amounts of ionising radiation are good for you as they could activate repair mechanisms that protect against disease. Even if there is not a beneficial effect, we know that there is not a drastically bad effect. Follow-up studies of patients who have had CT or PET scans and also studies of workers such as radiologists or radiographers, who have had higher than average exposure due to the nature of their jobs, have found no conclusive evidence of adverse affects. Nevertheless, there is uncertainty, and so the number of PET and CT scans that one individual can have should be kept low, whereas MRI can be repeated as often as you like.

MRI, however, is not without risk. Very strong magnetic fields are used and so metal objects that are inadvertently brought into an MRI room can become powerful missiles. Try holding a nail close to a small bar magnet. With the large magnets used for MRI there have been fatalities, but they are a result of malpractice rather than an inherent biological risk of the technique. Perhaps not surprisingly, compensation law firms are starting to latch onto this as a source of income. Very tight procedures are required around MRI scanners.

Medical ULTRASOUND scanning

It should come as no surprise to learn that medical ultrasound was first developed in Glasgow. In the 1950s the shipbuilding industry was flourishing, and like many big industries, smaller businesses grew up around it. One of these was Kelvin and Hughes Ltd. In 1946 Henry Hughes had set up a company to make pulse-echo metal flaw detectors. In 1947 he amalgamated with the Glasgow firm, Kelvin Bottomley and Baird, to form Kelvin Hughes Ltd. They worked to improve the metal flaw detector by using a higher frequency of ultrasound and so get better resolution.

Across the city, in 1954, changes were taking place within the University of Glasgow. They were going through a 'modernisation' phase and looking to improve their faculty of medicine. They were recruiting only the best. One of the best was Ian Donald, who had completed his training at St Thomas's Hospital in London and was at the time working at the Hammersmith Hospital. Donald had been in the Royal Air Force during the war and so was familiar with many technologies. In a development that bears many similarities to that of CT scanning by Godfrey Hounsfield twenty years later, Donald used his knowledge, and also his determination, to devise and test the first medical ultrasound scanner.

Like most developments, the initial designs had to go through many iterations before devices that could image internal organs were produced, but Ian Donald was not one who would give up easily. By 1957 he had developed an ultrasound device that could distinguish between an abdominal cyst and a solid tumour. This was published in *The Lancet* [12], in an article by Ian Donald, John McVicar and Tom Brown, the latter being an employee of Kelvin and Hughes Ltd. It is interesting that this partnership between a University and a Commercial Company formed without having a nationally supported Innovation Centre. They were just left to get on with it. Shortly after this the technique was used to produce the first ultrasound images of a fetus. The full account of these developments by Malcolm Nicolson and John E E Flemming is well worth reading [13].

We now take medical ultrasound for granted, in particular fetal ultrasound. Expectant mothers are examined at regular intervals and irregularities in fetal development or positioning can be detected at an early stage. The quality of images has improved enormously over the years. Ultrasound was never one of my specialist fields, and I always needed an interpreter when looking at images. You don't need nearly such a trained eye now.

The physics of ultrasound distinguishes it from CT, MRI and PET. While the latter three use what is called electromagnetic radiation, ultrasound is high frequency sound. The way we illustrate electromagnetic radiation is with waves going from side to side, whereas sound waves move longitudinally. Electromagnetic radiation can travel through empty space, whereas sound needs atoms or molecules to bounce backwards and forwards. Like MRI, which uses radiofrequency electromagnetic radiation, ultrasound does not affect cells in the body, at least not at the intensities that are used in medical scanning. However, recently, a new application is developing where very high intensities of ultrasound are used deliberately to burn out small regions. Currently small tumours, for example, can be removed by surgery, or by radiotherapy using high intensity beams of X-rays or protons. The new technique, called HIFU, High Intensity Focused Ultrasound, aims to do this with ultrasound. It is already being used in the treatment of prostate cancer and its use is likely to spread to several other applications.

Instruments that combine ultrasound and MRI are now available. In yet another spin to MRI, it has been shown that the rate of loss of the spin signal is affected by temperature. When high intensity ultrasound is focused on a small region it will start to heat up the tissue. MRI can measure the temperature change and thereby determine when the ultrasound beam should be switched off. This is such a good idea. As well as being used to treat tumours, it is being proposed that the technique could be used to remove parts of the brain that aren't working properly and causing seizures in epilepsy or tremor in Parkinson's Disease. The results of clinical trials are eagerly awaited.[1]

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At normal intensities, diagnostic ultrasound scanning isn't much use in the brain as the skull absorbs most of the signal. In a developing fetus this isn't such a problem as the skull isn't fully formed, but in adults the signal is too weak. There is, however, one exception. In 1982 Rune Aaslid developed a technique to measure the velocity of blood flowing in major arteries inside the brain. It's called Transcranial Carotid Doppler or TCD. Carotid is the name of the artery in the head and neck, and Doppler is the name of the process whereby sound frequency is altered by the movement of the object that emits the sound or reflects it back to the detector. You might have experienced this with jet planes, police cars or train whistles. Objects moving towards you have a higher frequency than when moving away from you. When an object coming towards you emits a sound, the waves are squashed a little and have a higher frequency and going away they are stretched. The faster the speed, the greater the frequency shift. Your speeding ticket might be a consequence of a measurement of the Doppler shift as your car passed the radar detector.

This effect can be used to measure the speed of blood in arteries in the brain because of an anatomical irregularity. There is a thin bit in the skull called the fontanelle. This allows the skull to deform during birth and it never develops to the thickness of the rest of the skull. So, it can act as a window that allows enough ultrasound signal to penetrate into the brain and this can be used to detect the frequency shift caused by the movement of blood in an artery. If something is obstructing the flowing blood, such as a lump of fatty material, then the blood passing through the narrow opening will go much faster. You can see this effect at narrow parts of a river, where the water flow can be very fast. A fatty deposit in an artery in the brain is likely to lead to a stroke. The larger it is, the faster the speed of blood flowing past it. This gives doctors a clear indication of severity and likely risk to the patient. It's true that you could see the fatty deposit on a CT or an MRI scan, but with a TCD instrument you can make the measurements at the bedside and repeat them as often as required

The developer, Rune Aaslid, is a Norwegian engineer who worked in Berne in Switzerland. I had the pleasure of meeting him at a conference in Cambridge. At the time his technique was well-established and his company, Hemodynamics AG, had been in existence for many years. He is to TCD what Ian Donald is to fetal ultrasound. I was struck by his unassuming modesty, and also fascinated, but not surprised, to hear that he still loved tinkering in his garage and making new devices.

[1] One of the problems with books like this is that they can be out-of-date before they are released. It has just been announced that a modification to this method using only MRI to manipulate tiny magnetic beads and then heat them using RF energy could be available in around five years.

CHAPTER 2: SPIN with DOCTORS

Medical Physics in the NHS: The Department of Clinical Physics and Bioengineering

Although I worked at the Institute of Neurological Sciences, my employer was the Department of Clinical Physics and Bioengineering [DCPB]. It is a specialist Centre, but specialising in the technologies rather than a particular clinical discipline. It wouldn't have been sensible to have tiny medical physics departments in each hospital. The model of having a large regional department that seconded staff to hospitals as required made much more sense. The person who first realised this in Scotland was John Lenihan. He was the pioneering physicist who set up a Medical Physics Department at the Western Infirmary in Glasgow in 1948. It became the Department of Clinical Physics and Bioengineering [DCPB] and now employees around 350 scientists and technologists. I don't intend to chronicle the entire history of this organisation but it is central to many of the anecdotes in the diary. Later I'll reflect on the two pioneers of Medical Physics in Scotland, the two Johns, Lenihan and Mallard, and how they developed slightly different models for the provision of medical physics services. Here I'll discuss the Glasgow model, which had to provide clinical physics services for hospitals serving a population of over 2 million.

I have mentioned that seven health-service restructuring exercises took place while I worked for DCPB. I'll not agonise over the details, but the changes were mainly around size. When I started I was employed by the West of Scotland Health Boards. It then became smaller. At one stage it was the Southern General Hospital NHS Trust. Then it started to grow again to allow for mythical economies of scale and eventually became the Greater Glasgow and Clyde Health Board. Management structures changed constantly and grew constantly. Within this sea of change DCPB managed to morph and continued as a single entity. I think that this is significant. When the original West of Scotland Health Boards fragmented there was an opportunity for senior ranking physicists to set up on their own and become leaders of new Departments. This didn't happen. Instead, a few grandiose titles were invented to accommodate the changing settings. We had regional physicists, area physicists, assistant area physicists, divisional heads and so on, but throughout all the turmoil DCPB remained intact. For example, there was no attempt to establish the Southern General Hospital Medical Physics Department as a separate entity. Why?

Perhaps the answer is best summed up in a statement attributed to the Chief Scientific Officer to the UK Department of Health in 1990: *"Physics services covering a single small district rarely make economic sense; the intellectual and professional isolation of a tiny group of Physicists is an even more serious mistake in the long term".* It was recognition of the value of regular intellectual exchanges with colleagues and the flexibility to shift from one job to another as demand changed that were the main binding forces that kept DCPB intact. The Department had excellent central electronics and mechanics workshops where specialised equipment could be repaired and where prototypes of innovative devices could be designed and assembled. It had regular seminars where ideas could be debated and ran teaching courses where we could draw on physicists with a range of specialist skills. Also, importantly, it had professional muscle, and could ensure that medical physicists had input to major Health Board decisions. Size matters. A few hundred was a good size for this type of activity. We had shared facilities and also a sense of belonging.

Medical physicists can have important roles in the routine delivery of healthcare, but perhaps their greatest value is in medical research and development. Working alone they could achieve very little, but in partnership with a few other professionals they can become important members of teams that strive to make advances in our knowledge of clinical disorders and in their treatment. Perhaps my passion for research comes from the ethos of DCPB when I first joined. The thought of a scientist working in the NHS and not being involved in research was anathema to the likes of John Lenihan. In the 1970s and 80s technologies were flooding into healthcare, but what was the point if they weren't going to improve treatment and advance knowledge? The widespread advances in the use of technologies went hand in hand with a growing emphasis on research and innovation.

Examples of Medical Technology Innovation

Innovation distinguishes between the leader and the follower.

Steve Jobs

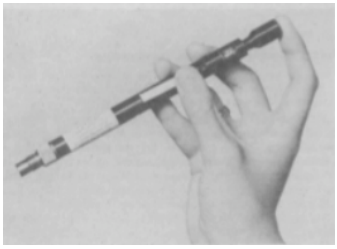
Many of us get good ideas for the development of new technologies. The challenge is to do something about it and convert the ideas into products. We have already looked at the development of CT by Godfrey Hounsfield and medical ultrasound by Ian Donald. It was perhaps their dogged determination that was responsible for the ideas becoming reality, but they were fortunate to be in settings where they could exploit this. In the 1980s the Department of Clinical Physics in Glasgow was an ideal setting for technology development. It was large enough to ensure that there was a plethora of doctors who might come up with problems that needed to be solved, and it had the facilities and expertise to take the potential solutions forward. I could be challenged on the assertion that it's generally doctors who come up with the ideas, and perhaps justifiably so. Ideas tend not to come to one individual in isolation. They come from observations in clinical settings and are molded by the discussion of possible solutions. You need a setting where ideas can be bounced around. We had that. Here are a few innovations that came from the Department of Clinical Physics in Glasgow.

The Insulin Pen.

As a contributor to the Medical Physics Technology course at Glasgow Caledonian University I was invited on one occasion to the Chancellor's Dinner. Just before the meal was served the lady beside me reached into her handbag, produced a pen-like device, and gave herself an intramuscular injection. She was diabetic. She turned to me and said, *"I don't know what I would do without my pen."* It was with great delight, and I hope not too much smugness, that I told her that the first insulin pen was developed in the Clinical Physics Department where I worked.

The idea came from a clinical team led by Dr. John Ireland, and the pen was designed by engineer John Paton. After several modifications to the original design a device was ready for clinical trial [15] and after a few further modifications the end product was at a stage where it could be passed to a company so that it could be made more widely available. This was in 1981.

The initial commercial device was called the Penject and was manufactured by a UK Company called Hypoguard, but the marketing rights were soon transferred to the pharmaceutical company Novo that had access to the global marketplace. It became the Novopen. The device was given away free, but of course would work only with Novo's insulin capsules. However, Novo still had to buy the pens and the Health Board made substantial royalties for many years.



The first pocket insulin syringe

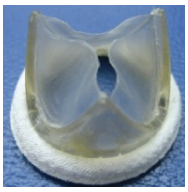
All this happened long before Intellectual Property policies were developed. The inventors were not rewarded financially and I was not aware of any of the income received by the Health Board going to the Clinical Physics Department, although perhaps some of our requests for additional funding were favourably received. I'm sure that the inventors would have accepted a share of the royalty income if an Intellectual Property policy had been in place, but I suspect that the feel-good factor that they would experience every time they met a user of the NovoPen would mean far more than money.

The Glasgow Heart Valve

In the 1990s we worked with David Wheatley, Professor of Cardiac Surgery at Glasgow Royal Infirmary. David had two traits that I remember well. He liked to operate to the sound of classical music and he was very innovative. We worked with him on a project that was to lead to the Glasgow Heart valve. He and his fellow cardiac surgeons were concerned that they had to replace valves too frequently. They were wearing out after

only a few years. Heart valves are designed to mimic a natural valve and can be constructed either from natural substances such as bovine pericardium or synthetic materials. David was sure that they could be improved by altering the design of the leaflet.

John Fisher was a graduate mechanical engineer in DCPB and was working on a PhD project. He had the skills and Prof Wheatley presented the challenge. How could the shape of the leaflets be modified to reduce wear and tear? Theoretical models were devised to study stress and strain, but before they could be used on patients, various valve designs had to be tested in practice.



This could be done in animals, but it would take many years before any flaws in the design would show up, so devices called pulse simulators were developed. They have tubes and compartments that mimic the heart and blood vessels, and a pump that can speed the process up considerably so that results can be obtained in months rather than years. Of course, this is far from perfect as rapid movements can amplify the wear and tear, but it does enable different designs to be compared to see if the new design is better than the original.

The project was successful. John was awarded his PhD, and the valve went into commercial production thanks to two entrepreneurs, Gordon Wright, an electrical engineer, and Eddie McDaid, an accountant, who had set up a company in Lanarkshire called Biomedical Systems. In this case both the Health Board, through the Clinical Physics Department, and the University of Glasgow, the employer of Professor Wheatley, benefitted from royalties.

A Powered Standing Frame

In many rehabilitation settings it can take several nurses or physiotherapists to get patients into a standing position, but it is important to do this. Being in an upright position improves bone integrity, keeps the heart active, is good for bowel function, can improve a patient's range of movement, can reduce the likelihood of bed sores, and has a general feel good factor compared to lying in bed for long periods.

In the 1990s mechanical engineers in our Department set about tackling the challenge of designing an automated device that patients could control themselves. They were not alone, but their model worked extremely well and benefitted from feedback from several rehabilitation specialists. We set about making it commercially available and thought that Remploy would be an ideal partner for this. This was an organisation based in a factory to the south west of Glasgow that provided employment for disabled people.

Sadly, soon after our efforts to set up a production line started, the Remploy facility had to close through lack of funding, and we were back to square one. We chose an unlikely commercial partner. Miranda was a mechanical engineering company based in Paisley to the west of Glasgow. They specialised in repairs to yachts, so had the technical skills and facilities, but they didn't have the market outlets or know-how to work in clinical rehabilitation. However, their CEO, Bill McAnally (seen in the illustration) was extremely enthusiastic and a subsidiary company, Insignis, was set up. Standing frames were manufactured and are still being sold today by Broadberry Care (Insignis) Ltd.

The EasyCom

I'm not sure if the name was inspired by the 1967 Elvis Presley movie, but the device that first introduced me to commercialisation within the NHS was called the EasyCom. I was not involved in identifying the clinical challenge or in solving the problem, so I'm entitled to describe it as a brilliant project. Doctors had become accustomed to doing ward rounds in geriatric units and shouting at each patient as they moved from bed to bed. They would often despair. *'That patient's a silly old fool. Why can't he plug in his hearing aid?"* Well, perhaps because he's old and you're not. Why don't you carry round a device that will amplify your speech and make it easier for the hard of hearing to decipher what you're saying?

The Easicom did precisely that. It was like a hearing aid, but instead of being worn by the patient, it was carried around by the doctor and used when required. The headphone would be passed to patients if they needed it. The device amplified the higher frequencies to account for age related deterioration. The Easicom worked well, was widely used and was marketed.

You might think that there was nothing special about this. Surely it was just a hearing-aid. And, indeed it was precisely that. What was special was that control had passed from the patient to the doctor. It was the doctor who had to switch it on and hand the earpiece to the patient. What was special about the Easicom was that it was designed to meet an every-day clinical need. The doctor didn't have to shout and so conversations between doctors and patients in geriatric wards could be a bit more private than they had been previously. The device improved the dignity of patients.

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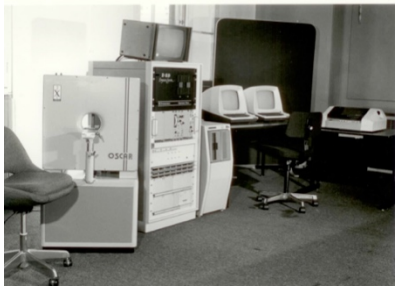
OSCAR: the bone scanner

'OSCAR brings a ray of hope.' That was the headline in the Evening Times on Thursday April 7 1983.

The rays were gamma rays and the scanner was designed to measure bone density more accurately than currently available devices to enable the effectiveness of new treatments for osteoporosis to be assessed in a few months rather than a few years. OSCAR stands for OSteometric Computer Assisted Reconstruction. All those who understood the explanation of CT would understand how it works. It was essentially a miniature CT, designed for the forearm rather than the whole body. There was one slight difference in that OSCAR used low energy X-rays from a radioactive isotope of iodine rather than the X-ray tube in conventional CT scanners.



OSCAR is on the left. To its right is the computer, which would now fit into your pocket. The forearm is placed in the hole in centre of the scanner.

Funding for the development came from Tenovus-Scotland, a small local medical charity, and this was matched by the Scottish Home and Health Department. It took 17 months to develop, worked well, and was then applied in clinical trials. Why didn't it hit the market like the insulin pen and bring royalties to the NHS in Scotland? The answer is quite simple. Although scanners like this weren't commercially available when the work started, commercial manufacturers were aware of the gap in the market, and they had a head start when it came to marketing. Developing a product can be much easier than getting it to market.

Innovative developments like this are still taking place within DCPB, but let's have a look at the wider setting.

The setting to promote innovation

None of the developments were designed to make money. The Insulin Pen and the Heart Valve did bring in significant royalty income to the Health Board, but the reason for doing the work was to solve clinical problems. They were all undertaken some time ago, and it is perhaps interesting to

reflect on the setting. These developments pre-dated the current NHS management regime. There were no performance indicators. Our Department did not receive a directive from the Health Board stipulating that we had to come up with X commercial devices or an income of £Y million from commercialisation. The Department was seen to be doing effective work that was benefitting patients and on occasions local industry as well. That was good enough for the Health Board officials. We have already seen that the main contribution of EMI to the development of the CT scanner was to keep out of the way: to employ Godfrey Hounsfield and let him get on with it. That was true of Glasgow Health Board in the 1980s and 1990s, but politicians would never allow a system like this to run today. No promises, no performance indicators, no targets, just allow employees to express their natural urge to do their best for patients. This work was not done by people who wanted to work a nine-to-five job. The developments were done by staff who were passionate about their work, who were not happy with the limited technologies that were available, and who wanted to make a difference. They were trusted.

So, if innovation could take place with Clinical Physics Departments, could it happen more widely in the NHS? That was the objective of *Scottish Health Innovations*.

Scottish Health Innovations Ltd. – SHIL – see also www.shil.co.uk

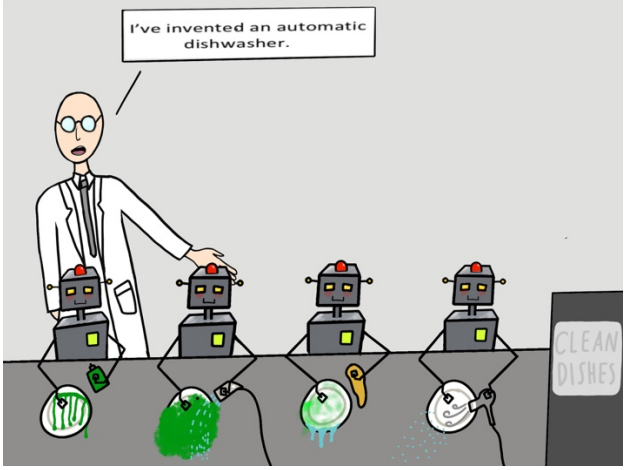
If you work in a clinical setting you are quite likely to get ideas about how to develop new devices or to improve on existing devices. This was the backdrop behind the establishment of Scottish Health Innovations Ltd - SHIL. It was set up in 2002, with support from the Scottish and UK Governments, in order to advance the commercial development of ideas originating within the NHS. I was heavily involved in the work of SHIL. I liked the concept, probably because this was the type of work that I'd been involved in for many years, and it was good that a national organisation was being established to support it. SHIL went on to attract EU funding, a door that has sadly now looks likely to close. Today, fifteen years later, it is still going strong. Formation of spin-out companies is not the only way to measure success of this type of organisation, but it is one indicator, and SHIL has so far helped to set up six. Frequently setting up a spin-out company is not the best route to market. An alternative to setting up a new company is to boost the production line of an established company and make use of marketing opportunities that have already been established, but perhaps the benefits of this are harder to quantify.

Physics and chemistry.

Medical Physics is a broad field. Shifting from one specialization to another is less common now, but in the earlier days it happened quite often. Working with clinical chemistry automatic analysers was another spin in my career.

At that time automation in chemistry was taking off and there were many innovative designs. The spin in clinical chemistry analysis was not just about centrifuges. New devices were starting to be used in hospitals around the world. I moved within the Department of Clinical Physics for a short period to take on a new challenge. One of my colleagues, Dr David Porter, had, like me, a PhD in physics. However, David had been faced with challenges in quite different fields – clinical chemistry and skullduggery!

Hospital clinical chemistry laboratories in the 1970s were using two distinct types of auto-analyser. In 1973 the Swiss company Greiner brought out an automated fully selective chemistry analyzer. Rudolf Greiner's background was in the watch-making industry and so when he turned his attention to the design of an automated chemistry analyzer the resulting product had many cogs, wheels and moving parts. It worked along similar lines to the manual methods, but the laboratory technicians were replaced by levers and conveyer belts. This worked well. In fact, it is still working well. The company is still in business and still innovating.



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The other type of auto-analyser worked on the continuous flow principle. These analysers were marketed by a company called Technicon. The principle employed was that a stream of material in a tube was divided by air bubbles into discrete segments in which chemical reactions took place. A continuous line of tubing passed the samples along several pieces of equipment, each providing a specific function such as distillation, dialysis, ion exchange, heating, incubation and recording of signals. The Health Board in the West of Scotland had invested heavily in Technicon auto-analysers and became very reliant on them. The trend had started. Machines were replacing people. Productivity increased and costs went down. Win, win; unless of course you were one of the laboratory technicians. However, the effect at that time wasn't too bad, as technicians could transfer to new more specialised analyses that were being discovered and were either too complex or too specialised to merit automation. It was a time of expansion.

However, as every car owner knows, automation goes hand in hand with maintenance, and continuous flow auto-analysers needed a lot of maintenance. Hence the skullduggery. Realising that they had a virtual monopoly in the maintenance of their products, Technicon started to increase their charges. The Health Board officers appreciated the benefits of auto-analysers and they marveled at the mechanics. However, there was one mechanical movement that troubled them. They were being screwed! What could they do about the escalating maintenance costs? Well, what were Medical Physics Departments for? They approached our Department and the end result was that David was called in to set up what became known as the 'Technicon Team'. David persuaded Technicon to train our engineers or else different auto-analysers might be bought in future. Once it had been set up this scheme saved the Health Board around £100,000 per year; a good use of taxpayers' money [16].

However, the Technicon auto-analysers soon ran into other problems. The electronic units that worked out the answers from the various measurements were starting to break down. The solution was fairly clear. This was at the start of the computer revolution, so it made sense to replace the old electronics with computers. This sounded simple, and it was, apart from the problem that often confronts scientists. Where was the money going to come from to undertake the development work? This turned out to be far from straightforward. Research Councils, generally the source of funding for academics, quite rightly didn't see this as an academic issue; and Health Boards don't fund commercial developments. Today there are government funded schemes administered by bodies such as Innovate UK that support precisely this type of development, but they weren't around at the time. There was, however, a company called Advanced Medical Supplies [AMS] that produced components for Technicon analysers at competitive rates. They were keen to work with us but didn't have the capital to finance the development. What was required was a bank loan. So instead of writing a grant application, I had to help to write a business case and appear in person with the CEO of AMS in front of a bank manager. This was a new experience and turned out to be a very pleasant one. I was very impressed with the speed at which the bank manager grasped the technical issues, and even more impressed that he agreed to provide the loan to AMS that we needed to design and construct the computer-based data processor.

When I look back on this episode what really impressed me was the efficiency of the exercise. Today, when academics apply to one of the funding councils or major charities for grant funding, the process can take up to one year. There might be a preliminary round to short-list typically around 40% of the applications, and these will then go forward to round two. Those going forward might receive comments from reviewers and adjust their application accordingly. The applications would then go out to peer review. As peer review is a grace and favour process undertaken by busy people, it takes time. A final list would be drawn up and then a proportion of these would be funded. Typically, around 20% of the original applications end up being supported. The process of getting a bank loan took around two weeks. Would I have liked it as much if the answer had been 'No'? I think I would. Clearly, I wouldn't have liked the answer, but we would have been able to regroup quickly and make other plans. Are our R&D funding processes efficient?

The project to develop new auto-analyser control units was reasonably successful. They were produced, and they worked well. We all know the pressure that is now put on us to buy new computers, phones and cars to keep pace with developments in technology – and to pay more money. Our clinical chemistry analyser control units helped to extend the use of continuous flow analysers by a generation [17] by letting us keep the reliable parts, the mechanical pumps and tubing systems, and replacing the obsolete parts, the outdated electronics.

Lecturing

Before I came here I was confused about this subject. Having listened to your lecture I'm still confused, but on a higher level

Enrico Fermi

Part of our work in the Department of Clinical Physics was to lecture to trainee staff. Generally, this involved sitting down with small classes of three or four, that being the annual intake of new recruits. The intimacy of this setting meant that it was easy for us to ensure that all were keeping up and understanding what was said. I mentioned earlier that when I was a new recruit there was no formal training course in medical physics. On top of that, few of us had any formal training in lecturing. I think that starting off with very small class sizes helped us on our way. The sessions were interactive and if anyone wasn't understanding what was said it was immediately apparent. Work had to be done, generally in the evenings, preparing the lecture material, but having done that, the rest was quite enjoyable.

After this inauguration, I had the pleasure of lecturing on various aspects of medical physics at each of the three Universities in Glasgow. The University of Glasgow is the oldest of these. In fact, it's very old, founded in 1451. There are plaques on the walls of the City Hall in the Candleriggs district of Glasgow to acknowledge the original donations when it was first built and one of these says simply "*The University*". The thought of another University in the City was anathema, and maybe still is to some Glasgow academics!

As medical physics was a rapidly expanding field the senior academics who had put together the syllabus for the honours course in what was then called Physics and Astronomy decided that it would be good to include medical physics, and we were invited to deliver the lectures. My method, and I think that of most of my colleagues in medical physics, was to prepare handouts covering the material to be covered and to give these out in advance. They cited reference material in textbooks and research papers and also had brief explanations of the topics to be covered. I showed slides and saw no need to scribble on blackboards or to include detailed mathematical problems that had to be solved. The objective was for the students to understand how the technologies worked, with an emphasis on the physical principles. Mathematics was seldom helpful in that process. It's not that we didn't use mathematics in medical physics, but it tended to be at a more advanced stage of application and not in understanding the basics. Mathematics was essential in teaching atomic and nuclear physics but was generally not an aid in understanding the applications in medicine. So, there were few equations, and no need to scribble on the board as the handouts and slides contained all the material.

I think that the students enjoyed this, but it didn't go down at all well with the janitors who were responsible for wiping the boards at the end of each lecture. As the students were leaving the lecture room the janitor would walk in, cloth in hand, and come to an abrupt halt, staring at the blank board. He would then look at me with a pained expression on his face, implying that he felt that I hadn't done any work. There was nothing on the board. How could that happen? If there were ten lectures in the series, this would happen ten times. By the tenth lecture I was getting a vigorous shaking of the head and a distinct '*you'll never learn'* look.

I also had the pleasure of lecturing on medical imaging at the University of Strathclyde. This is a much newer University, formed from the old Technical College in 1964 as the first technological university in Scotland. From our perspective we found this to be a good setting, perhaps because our lectures were in the applied physics course, and medical physics is precisely that.

The lectures at both these Universities proved to be invaluable for the recruitment of trainee medical physicists. We could frequently spot the likely applicants early on in the courses. They were the ones who asked questions, and who were interested and enthusiastic. It is very rewarding when this

happens, and you can track students through to employment and then through the ranks as they progress. This progression can be local, or far and wide.

In 1993 a third university was established in Glasgow, Glasgow Caledonian University [GCU], and we were also involved in teaching there. The objective was to work with students who might go on to pursue a career as medical physics technologists. The NHS needs more technologists than scientists. To oversimplify the distinction, scientists work on the development and implementation of technologies and technologists work on the repair, maintenance, setting up and routine use of technologies. When I first started in medical physics technologists were employed by the NHS and sent on a day-release basis to colleges where they learned about the theories underpinning electro-medical devices. This worked well, but the trend in the late 1990s was to set up more and more university places and so colleges morphed into universities.

GCU is very good at what it does, and our courses there were very successful, delivering many excellent technologists into the NHS, but the political move to set up more universities was an unmitigated disaster. Instead of pretending that most people need an academic education, why did we not simply improve the status of colleges and attach more value to the skills of artisans. This is yet another example of spinning in the wrong direction - of the constant urge to reorganise. Business leaders in the UK now complain regularly about the inability to recruit skilled craftsmen and our manufacturing industries are suffering as a result. The technical college day-release process was successful because it gave young recruits a good work ethic and at the same time they had the opportunity to study the theory behind the technologies that they were encountering. Unfortunately, leaving something alone doesn't go down well in politics.

Personally, I felt bad about my role in the move toward a graduate education for medical physics technologists. I was one of those pushing for the establishment of the Medical Physics Technology degree course at GCU. Many of my colleagues were critical of this, and I could understand why. I was advocating that the system that they were familiar with, and that had worked so well over the years, was going to be replaced. The problem was that the NHS had pay levels that were linked to entry requirements, and unless medical physics technologists could match other technologists in the NHS and had university degrees, then they would be put inappropriately on lower salaries. So, I had to back a move that I was very uncomfortable with. It was one of many examples of reorganisation in the NHS. Let's have a closer look at this.

Chapter 3: ORGANISATIONAL SPIN

"We trained hard, but it seemed that every time we were beginning to form up into teams, we would be reorganised. I was to learn later in life that we tend to meet any new situation by reorganising; and a wonderful method it can be for creating the illusion of progress while producing confusion, inefficiency, and demoralisation."

Charlton Ogburn, Jr. (1911-1998)

I'm about to embark on a series of moans. At my age it's your role in life to be a curmudgeon. I've tried, however, to make constructive suggestions.

Healthcare Systems, redisorganisation and bureaucracy

I have far too many research papers stashed away in drawers and cupboards, but pride of place goes to an article published in 2006 by authors from Norway and Canada entitled "*A surrealistic mega-analysis of redisorganisation theories*" [18]. It references a similar paper by Smith and colleagues published in the British Medical Journal in 2001, also pointing to what they call 'redisorganisation', in this case within the NHS [19]. This is a classic example of organisational spin. The articles focus on healthcare systems, but I suspect they are of much wider relevance. The central issue is that reorganisation, or as they understandably title it, reDISorganisation, is now endemic within our working practices.

It would be very unscientific to resist change. We are always learning and should always be willing to change our systems of work and the infrastructure that supports them. The challenge is to do it well, and not just for the sake of doing it.

I experienced seven redisorganisations while working in the NHS in Scotland. It started out with the massive West of Scotland Health Board, a body that covered the whole of west Scotland. Gradually the territories became smaller until we ended up in the 1980s with the Southern General NHS Trust; a single hospital with its own budget. Then it started to grow again.

The Southern General Hospital had an interesting history. It dates back to 1872 as a 240 bed Poor Law hospital combined with a 180 bed lunatic asylum. It is now the Queen Elizabeth University Hospital with 1,109 patient rooms. Working there in the 1980s was a privilege. You identified with the place. The Chief Executive, or fat controller as he was affectionately known, was respected far and wide. He came to the annual Southern General Fair and sold umbrellas to raise additional funds for the hospital. If there was any negative publicity about the hospital we took this personally, even if it was nothing to do with us directly. It was our team.

Then, however, the vastly over-rated concept of 'economies of scale' started to creep in and reorganisation was inevitable. The size of the NHS compartments started to grow and after a few interim stages the end result was the Greater Glasgow Health Board, soon to be followed by the even larger Greater Glasgow and Clyde Health Board. In the NHS reorganisation is never very far away. Some of these systems were better than others, but they all worked to a greater or lesser extent, so what's my problem? The main issue is that each of these changes was an example of redisorganisation syndrome, and the spread of this condition is something that healthcare professionals have been unable to stop. Reorganisation is now big business. Frequently it's a defense mechanism. '*This is awful. What are you doing about it?' … 'You're right. We'll completely reorganise the service'.* A completely new structure will be proposed. Departments will merge. *There will be economies of scale. The new management structure will be more efficient.* However, it will be too big for a single tier of management, so we'll need more middle managers. But this extra cost will be offset against improved efficiencies in service delivery. And so it goes on.

Politicians are perhaps the worst offenders. Reorganisation - or as they often brand it, reforming - appears in all manifestos. I'm not advocating for one minute that change is bad. What I take issue

with is that the reformation processes are so unscientific. In science we advance knowledge a little at a time. We conduct pilot studies to see if we are on the right track. We publish our data, making it openly available to the peer community who can comment and influence the future direction of travel. If the pilot data look promising then we conduct a larger study to gather more information, and so on. We learn from the successes and failures of others around the world and make informed changes - one step at a time. We criticise our own work. We feel our way gradually. Even if someone has a completely revolutionary theory, this has to be built up gradually in manageable steps. This is the responsible way of making progress. Tweaking rather than bulldozing.

The widespread practice of resorting to radical reorganisation is usually a leap into the unknown, but that's not the only problem. Each episode leads to years of inwardly focused activity. Time and effort that would otherwise have been devoted to exploring problems like why some stroke patients recover better than others, or why some head injured patients deteriorate so rapidly, has to be devoted to attending meetings about the new divisional structure or the new allocation of laboratory space. Navel-gazing has replaced star-gazing. Our focus is directed inwardly rather than looking out to the world and having time to take part in the global advancement of healthcare.

We are experiencing this in the UK just now, when all our focus is on leaving the European Union. Whether or not you support leaving the EU, you have to acknowledge that it is one of the biggest acts of reorganisation in the UK in recent times. Entirely new legislative systems will have to be developed, and that will be a major focus here for many years. How many additional bureaucrats will be needed? What will all this cost? How much productive work is being under threat because of this? Will our place in the European research community, that we have all strived to build up over many decades, be lost? The EU was certainly broke and needed fixing. Long before the referendum was announced I listened to several presentations by non-UK EU officers who went on at length about the overelaborate bureaucratic processes and the need for reform. It had to change, but did we need so much spin; one of the biggest reorganisation exercises in recent times? Maybe in the long term the problems will ease out, but the decision to leave was made by a very small majority and was based on either absence of information, or the more sinister alternative of misinformation. Deliberate lies. The move to leave is not easily reversible and there was no accurate data to inform the voters. At least the election of politicians can be reversed every few years. Of course, we need regular updating of processes, but we need informed change and ways of filtering out misinformation. Could we have done that with the Brexit proposals? Probably not. So, from my biased position as someone who is passionate about scientific research I have to consider the decision by David Cameron to ask the country to vote on an issue on which we had very little true information must rank as one of the worst political blunders in recent times.

Bureaucracy affects morale within professions

I find it sad that many of the enthusiastic doctors and surgeons that I worked with over the years have now reached the position where they are desperate to retire. Having read two books by neurosurgeon Henry Marsh after he retired [20,21], and having had personal discussions with several ex-colleagues, I'm aware that there are special factors that affect neurosurgeons. The cases that don't work out keep coming back to haunt you. As one of my colleagues put it – out of every hundred operations ninety-nine might go well, but it is the hundredth patient who keeps coming back to your clinic with very severe mental difficulties. Often neurosurgeons have had to decide whether or not to operate. If they operate and there's a good outcome, then that will be very uplifting and rewarding. However, if all does not go well there could be a nagging doubt that the wrong decision was made. We all make wrong decisions, but the burden that neurosurgeons bear is particularly heavy, and in many cases, they reach the point where they've had enough.

However, when I discuss retirement with most other medical colleagues the common theme is utter dissatisfaction with current management practices, and in particular the ever-increasing micro-management, or as one of my colleagues in medical physics called it, *pico-management*. The problem is not managers, but management processes. This is a view that goes way beyond my circle of acquaintances. In a study led by researchers at the University of Oxford published in BMJ Open [22],

doctors who graduated in 1974 or 1977 were asked about retirement. The most frequently mentioned reason underpinning a decision to retire, cited by 45% of responders, was the impact of work-related bureaucracy.

The NHS is a business and it needs good management. I certainly don't adhere to the view that it should be managed entirely by medically qualified practitioners, although you do need a strong medical presence in the management team. Clearly, the management of such a complex organisation has to be entrusted to those with appropriate training. Managers are not the villains here. Many of those that I've worked with have been conscientious. Many, but not all, have had reasonably good judgement. The problem is that they are trapped. Trapped by political processes. The villains are politicians, for continuingly tinkering and setting up vastly complex bureaucratic systems, and us for voting for them. However, we can't take too much of the blame, because we have little choice. All political parties have the same failing. They see it as their role to micromanage public bodies. They do this by imposing ill-informed performance criteria; targets, threats, and an inherent urge to reorganise.

Performance Indicators are fundamentally flawed

You might wonder how I could possibly criticise performance indicators. We can't just leave staff to get on with it. It would be shambolic. No, we can't just leave staff to get on with it, although in most cases that would probably be fine, but current practices definitely need to be overhauled. They are quite simply not working. I have witnessed a growing focus on performance indicators over the years and there's little evidence that the NHS is more effective as a result. They do not always target the most appropriate factors in healthcare, it takes a lot of time and effort to record the data and more time and effort to collate the results - and these can be subject to spin. Reports of fiddled data appear regularly.

I came across an excellent example of an inept performance indicator system within our own Department. We had to make sure that all our technologists were pulling their weight. No slacking. So, we recorded the number of jobs completed by each staff member as part of our BS5724 quality standard system. Perhaps not to our surprise, the best technologist had stats that were way below the rest. He appeared to be by far our poorest performer. What was happening was that he was given all the really complex medical equipment problems to work on; the ones that few of his colleagues could handle. These took longer to complete and so he did fewer repairs, but he was the most indispensable member of the team. He was the one that others learned from. We didn't have a performance indicator that reflected quality, because it was harder to devise one. Many of the jobs that he completed were unique. There were no comparators. We all knew how good he was, but couldn't devise a measure to report this. *"Take our word for it – he's good,"* doesn't go down well in performance management circles.

So, do we just abandon performance indicators and quality systems? We clearly can't do that. What could be tried, however, would be to ease into processes that are less rigid, and to put more faith in professional integrity and general public feedback. I mentioned earlier that when our small hospital, the Southern General Hospital, was the subject of bad publicity (which I hasten to add didn't happened very often) we all took it personally. Even if the criticism was nothing to do with our own work, we felt bad. We had a sense of pride and a sense of belonging. The reputation of our hospital had been tarnished. I sense that this valuable performance enhancing mechanism has been lost in the NHS. We all have pride. It's natural and it's powerful.

There are encouraging signs that this is being recognised and at least some effort is now being put into encouraging good all-round performance and teamwork. There are various 'excellence' awards and big shows. However, a sense of belonging to the team should really be embedded into the framework of the organisation. Maybe this means that we need smaller groups and not large Health Boards. Does this also apply to multinational companies? From many discussions with employees in these organisations I suspect that it does. It's good to have team spirit, and the team needs to be fairly

autonomous if we are to feel that we really belong to it. We need to take pride in 'playing for the jersey'.

Then the team needs to present a true picture of its performance. Waiting lists and waiting times are important but the overall effectiveness of the treatment is surely more important and this links into how well recent research findings have been implemented. Devising criteria for informed feedback won't be easy, but we urgently need systems that reflect performance and do not require endless form-filling and collation of political showcase performance indicators. The cost-benefit of performance assessment processes has to be optimised. Every penny spent on collation of performance data is a penny not spent on employing more frontline staff.

Perhaps this could be set as a challenge for IT professionals, ethicists and social scientists to address. Maybe mathematicians might have something to offer. Could mathematicians following in the footsteps of Leonid Kantorovich and George Dantzig derive algorithms to enable efficient processes to be developed to maximize productivity and at the same time take account of feedback on performance? Importantly, the algorithms would have to factor-in the costs involved in getting the measurements of performance. This is a challenge that applies far more widely than to the assessment of health care systems, or large public bodies or companies. It's at the heart of our need in society to derive processes that optimise performance and at the same time react to user feedback. In many respects physics is much simpler than social science. We deal with stuff. Social scientists deal with constantly changing mindsets. But surely it is a realistic goal to expect that robust cost-effective performance assessment processes can be developed. We need them.

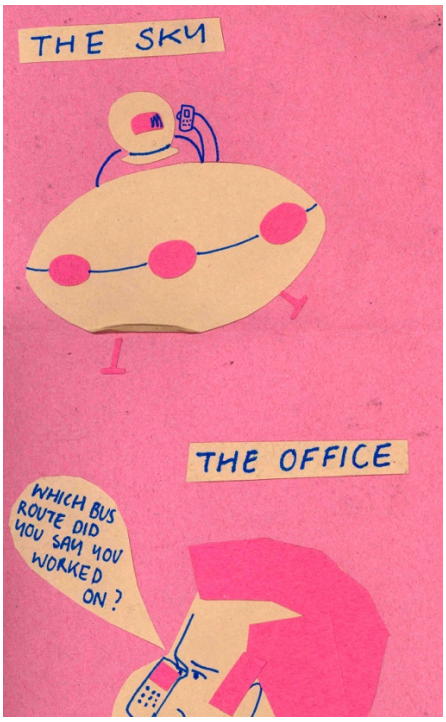
Work and the feel-good factor.

I described earlier a study to find the pleasure centres in the brain. Pleasure comes to us naturally, and perhaps this is overlooked in the workplace. How often do politicians campaign to make our work more enjoyable? In fact, many do quite the opposite. They campaign for shorter working hours and more holidays. The implication is that work is not enjoyable. Sadly, I meet so many workers in a wide range of professions who can't wait to retire. So how can employers help to make our work more enjoyable? It would be arrogant to suggest that I have the answers to this, but here are a few thoughts that might trigger discussions:

> **Performance bonuses.** There is no doubt that good medical doctors are the most important cogs in the healthcare wheel, but should senior doctors and managers in the NHS be rewarded with bonuses when there are no comparable awards for other grades of staff? A general problem with bonus systems is that they rely on performance criteria against which the awards are assessed, and these can be deeply flawed. For example, in 2016 it was reported that senior managers at NHS Tayside were awarded bonuses after getting positive grades for their performance, despite the organisation relying on bailouts from the taxpayer. The medical profession defends its merit award system, but surely what doctors really crave for is respect rather than money. Rewarding excellence is not a bad idea, but bonus systems would be more respected if the money went to the setting rather than individuals within the setting. So, for example, if the award is for research excellence, then put the money into the appropriate research fund. If it's for clinical excellence, then boost the funding of care facilities in the ward. This would boost respect for the individuals concerned. It can't be good for the morale of the majority of the workforce when a tiny, well paid, fraction have these artificial privileges.

Career Development.

We don't live in an era when a single skill-set is likely to see you through life. It's true that most professions now put a great deal of emphasis on Continuing Professional Development, but is it a box to tick or an effective process to develop new skills? For it to be really effective job descriptions have to be flexible so that the job can morph to accommodate changing demands on the service. For example, when MRI first arrived on the scene, several of the medical physics technologists jumped at the chance of adding to their skills and volunteered for retraining. They weren't paid any more, but they recognised that a new, exciting, technology had arrived and they were keen to learn about it and to work in that setting. They were role models.



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Reduce bureaucracy and micro-management.

Then came the churches, then came the schools
Then came the lawyers, then came the rules

Telegraph Road, by Mark Knopfler

It is simply no fun to have to fill out forms that you know are a waste of time. This has a massive effect on morale. Politicians, please do something about it. I read recently an article written by a senior officer in a Scottish political party boasting about the number of new pieces of legislation that the party had introduced. I would give Brownie points to the party that removed some of the less effective legislation. Of course, any civilized society needs rules, but the cost of implementing the legislation and the bureaucratic load need to be considered.

Perhaps one explanation behind having so many rules is that we appear to have a disproportionate number of lawyers in parliament. In 2015 119 out of 650 MPs in the House of Commons had either studied or practiced law. This contrasts with 26 with a background in science or medicine, and zero with a doctorate in science. In 2015 there were only three medically qualified MPs in the House of Commons. With the current bias towards those with a legal background it's hardly surprising that parliament has become a factory for the production of work for lawyers, and lawyers thrive on bureaucracy. I suppose it rests with scientists and doctors to do something about this, but we all have such fascinating jobs! So, politicians, please reduce bureaucracy, gather data on the benefits of what you've done, and then boast about it. That will get you votes.

Instill a sense of belonging. Whether it's a state run or a commercial organisation, size matters. Small is beautiful. If you need economies of scale, then collaborate. If it has to be a large organisation like the NHS, then the parts need to have sufficient autonomy to make every individual feel that this is their team. That's how I felt about the Southern General NHS Trust. It's not how I felt about NHS Greater Glasgow and Clyde.

Maybe readers could reflect on your own position. Do any of these factors apply in your workplace – past or present? Maybe they don't. Maybe it's just the NHS, or maybe it's just me. It would be interesting to know.

Chapter 4: Spinning out the money

What can the NHS afford to do? - The Health Technology Board for Scotland: HTBS.

It's no good praying to the powers that be
'Cause they won't shake the roots of the money tree

Paul Weller

Everyone involved in medical research is driven by a thirst for new knowledge, but the primary driving force is the awareness of our limited ability to treat many major illnesses. Waiting time initiatives feature in most political manifestos, but a far greater problem is that in many instances patients have conditions for which there are no effective treatments. It is critically important, both for the economy of the UK and the health of the nation, that we are at the forefront of the drive for new knowledge and more effective treatments. We need the right balance between investment in research and in health care delivery, and both involve deciding on priorities.

All healthcare systems around the world face an impossible task. The demand is infinite, and the available funding is finite. A common problem is that Governments set impossible targets by giving, the NHS too broad a remit. It's hard to say 'no' when you're trying to attract votes and so the remit keeps expanding. Nations have come up with different ways of structuring healthcare systems and the one common factor is that they are always under stress and always open to criticism. Healthcare systems are political pawns. They feature in every manifesto and, as mentioned above, are constantly being reorganised. In an attempt to make best use of finite resources a body called NICE [the National Institute for Health and Care Excellence] was set up in the UK – or to be more precise in England and Wales. In Scotland Health Care is the responsibility of the devolved Scottish Government and so the Health Technology Board for Scotland [HTBS] was set up, albeit briefly, before being spun into a different organisation.

HTBS was led by an excellent CEO, Dr Karen Facey, and chaired by Professor Angus McKay. Angus had been one of the leading research psychiatrists in the UK before moving quality of life to the top of his agenda and opting for the post of superintendant at the Hospital at Lochgilphead on the west coast of Scotland. Psychiatrists have to be good listeners, and so Angus was a splendid Chairman. I was appointed to HTBS as the technocrat, along with colleagues from public health, psychology and, importantly, health economics. I came to respect the expertise that they all brought to the table, but particularly the skills of health economists. Healthcare is implicitly a caring profession, and it can appear a bit heartless to bring in economics. However, we all know that resources for healthcare will always be limited and prioritisation is essential. So how do you prioritise?

The worst way is to be influenced by action groups and politicians. Those working in action groups are well meaning, but invariably biased towards their particular focus. Politicians are biased towards vote-gathering, and short-term outcomes that make headline news. Health economists are unbiased and deal with factual information, informed by worldwide knowledge of clinical practice. The first step is to integrate cost with clinical effectiveness. There are various ways of doing this, but the method that we adopted was to use what are called QALYs – Quality Adjusted Life Years. This is a measure of disease burden based on quality of life during the expected lifespan. One QALY is assigned to someone who has a year of perfectly good health and zero QALYs to someone who dies. Interestingly it is possible to get negative QALYs. Whether QALYs are used, or a similar system, this process is bound to be controversial. How do you define quality of life? It is very personal and very hard to assess. It is, however, perhaps the best that we can do. Whether we like it or not, our finite resources have to be distributed as fairly as possible, and both quality and quantity of life are key determinants.

HTBS had two roles. Much of the activity went into revisiting the recommendations of NICE for England and Wales and making any alterations that might be required in the Scottish context. The main issue for Scotland was that it's a bit more rural and that could be a factor in healthcare delivery. It seldom was, but it had to be considered. The other role of HTBS was to undertake its own health

economic evaluations. In its short existence it didn't do many of these, but one that I was particularly involved in was to assess whether or not PET scanning should be introduced into Scotland. I've already covered PET, looking at how it works and what it can be used for. The challenge facing the NHS in Scotland was to decide whether PET would be cost effective in particular clinical settings. It is an expensive imaging technique. Not only does it need a sophisticated scanner to produce the images, but it also needs tracer materials that have to be produced locally using very costly processes. So, is the expense justified?

At the time, Scotland didn't have PET in the NHS. There had been a University scanner in Aberdeen for some time, but none in the NHS. Should there be? PET has many potential applications. By using different tracers, very many physiological processes can be studied. However, it made sense for us to concentrate on the commonest tracer, FDG, in one of the most critical clinical settings, scanning patients with non-small-cell lung cancer. The question that was set was *'is the use of PET with the tracer FDG cost-effective in the management of patients with non-small-cell lung cancer?'* In order to answer this question, you have to look at all the processes within a patient's clinical management cycle, and when you look into this you find that there are many different approaches in different Centres. The literature has to be studied and the various options considered. In all, seven different strategies for patient management were compared in the HTBS evaluation and it was concluded that PET would be cost effective in Scotland. A process that included PET had more QALYs than one that didn't. The main benefit was that needless operations could be prevented.

The role of HTBS was to make a recommendation. It was up to others to implement this and it did take some time before PET was introduced to hospitals in Scotland, but it came eventually. One benefit was that, having been shown to be cost effective in one medical condition, it then became an easier challenge to spread the benefit to other conditions as start-up costs were no longer a factor. PET is now widely used in Scotland, as it is in all other developed countries.

There was still a challenge though. When introduced into the NHS the result was that surgery departments saved a considerable amount of money but radiology departments, where the PET was undertaken, spent a lot more money. So, the simple solution was that funding would have to be re-routed from surgery budgets to radiology budgets. I'm not aware of that actually happening. The debate had simply moved to a new battleground.

Now for some suggestions to improve the use of available resources and to tackle the bureaucracy overload discussed earlier.

Evidence based distribution of resources

Bodies like NICE were set up to provide guidance on the clinical and cost effectiveness of treatments. Its remit has stopped short of gathering unbiased evidence on the overall effectiveness of the NHS in different clinical settings. To take one example, are the QALY benefits of hip replacement better than those of surgery for brain tumours like glioma? Could health economic evaluation be applied across the NHS, or any healthcare delivery system that has finite resources? A scale could be drawn up to enable the available funding to be put to best use, and it could be informed by unbiased evidence of current practices around the world. Decisions would be removed from the whims and fancies of a few politicians and powerbrokers. Staffing levels at specialist Centres would be in proportion to demand and the distribution of resources for specialist training could be adjusted. It would all be evidence-based and, as it would be directed at optimising quality of life improvement, presumably it would also optimise the popularity of the NHS.

Of course, not everyone would like this, and there would certainly have to be flexibility to take account of other factors. In the treatment of conditions where there are recent promising research findings there might not have been time to build up an evidence base of clinical effectiveness. Perhaps, though, that wouldn't be a major problem as research funding would be supporting clinical trials in these areas. A bigger problem might be in fluctuating demand for services. Major disasters and outbreaks of infectious diseases put an acute strain on services and this would have to be factored in to the resource allocation process.

Could a system like this be influenced by spin? Could health-economic surveys be affected by the types of mis-information that are so common in news reporting? I don't think so. All surveys would be published in full and be similar to medical and scientific research papers. They could be peer reviewed and be amended if flaws are detected. As in the stock exchange, there would be short-term fluctuations as new data appeared, but in the longer-term, this process could be a robust reflection of the effectiveness of the healthcare system.

I'm surprised that Governments don't appear to have given this much thought. It would take a lot of pressure away from them as they could claim that the limited resources that are available from taxpayers' money were being put to best use, and that there are robust processes to prove that. There would still be many challenges. One of the first might be to train more health economists, but that would be a good challenge. It's a very valuable profession.

Evidence based costing of bureaucracy.

Could this be taken even further? I wonder if cost-benefit analysis could evolve to cover bureaucratic systems? We are always reading about the NHS not having adequate resources. This applies also to education, and most public services. It doesn't appear to matter which political party is in power. These services are always under-resourced. Well, they are, and they always will be. Healthcare can place an infinite demand on resources.

We have to prioritise, and also to ensure that the money that is available is being put to best use. In order to do this, we have to know the full cost of all components of the system, and we need a QALY-type measures that include the bureaucratic processes. Importantly, there should be a cut-off to eliminate or modify those processes that fall below an agreed threshold. It's not good enough to simply hide these as overheads and call it 'full economic costing'. We cost salaries of front-line staff, we cost equipment, and we cost consumables, so why shouldn't we cost bureaucratic processes? Recently the Harvard Business School computed that excess management is costing the US $3 trillion per year. Our current practice of accepting whatever bureaucratic processes are thrown at us needs more than a little spin. Even if we just set about measuring the costs, that would be a start.

Let's move on. A tried and tested way of improving the distribution of resources is to centralise high-tech specialised clinical services. I can think of a splendid example.

Specialist Clinical Research Centres of Excellence

The Institute of Neurological Sciences [INS] in Glasgow was a Specialist Clinical Centre of Excellence. That is excellence in medical science rather than aesthetics, as its 1960's architectural design illustrates. Appearance is a matter of taste, but appearance wasn't the main problem. The setting was 'enhanced' by a pond with fountains. Unfortunately, this type of ornamentation needs maintenance, especially in autumn, and relies on respect from passers-by who might have litter to dispose of. Neither was forthcoming.

It didn't last. Even more unfortunately, the vertical tiles on the walls were prone to coming loose. This could have been useful in boosting patient throughput in neurosurgery, but the tiles had to go. That made the building safer, and uglier.

The workmanship was also from the sixties. One benefit from working is a hospital was that we had showers in the changing rooms. I used to use these regularly after the run to work. On several occasions the shower proved to be counterproductive when I was showered with tealeaves from the sink in the kitchen above. The plumbers weren't the best, but fortunately the neurosurgeons were better when it came to repairing leaking blood vessels.

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Sadly, the problem hasn't gone away. A news article in July 2016 revealed that neurosurgery was being farmed out to the private sector because of a plumbing problem that led to raw sewage leaking down hospital walls. Eighteen leaks or floods in as many months had led to a backlog of operations at the ageing Institute.

When it opened, the Institute of Neurological Sciences [INS] was a regional specialist NHS Centre that incorporated University Departments and had many links with industrial partners. I suspect that we were regarded as elitist by other Departments, and maybe we were, but it was a thriving community. A feature that made this a very special experience for me was that I was in the presence of incredibly talented and enthusiastic colleagues from many disciplines. I had the privilege of working in a setting that had academic departments of neurosurgery, neurology, neuropathology and neuroradiology. Professors Bryan Jennett and Graham Teasdale already had world-wide reputations, and other such as Sam Galbraith [23] and John Pickard were on their way to establishing these. I was mixing with visiting scientists and doctors from around the world – USA, Canada, Australia, Japan…... Not only was I soaking up new knowledge about medical practice, I was also able to go on virtual tours of many countries by listening to their stories.

Graham followed in the footsteps of Professor Bryan Jennett as head of Glasgow University's Neurosurgery Department. He is perhaps best known as co-developer of the Glasgow Coma Scale or GCS [24]. This is mentioned frequently in medical TV dramas. You can listen out for it. *'The patient was admitted with a GCS of 9."* The concept of the GCS is simple. It is a way of recording the conscious state of a patient when admitted to hospital, typically a patient with a head injury. A GCS of 3 indicates deep unconsciousness and it goes up to 15, indicating no measurable deficit. It is based on simple clinical observations of eye responses, verbal responses and motor responses.

The main reason for developing the GCS was that research into the management of head injured patients was a mess. Publications contained lengthy descriptions of clinical observations and it was difficult to get a collective picture. Forty years after the original paper was published a survey [25] showed that the GCS is in use by neurosurgeons and other professionals in more than 80 countries worldwide and has been translated into the national language in 74% of these. The review also noted a continuing rise in the use of the GCS in research reports, making it the most frequently quoted paper in clinical neurosurgery.

One of the visitors to the INS set up an in-person international visit for me rather than a virtual tour. Larry Pitts was a San Francisco neurosurgeon who was spending time in Glasgow. He worked with me on cerebral blood flow measurement and asked if I would be willing to go over to San Francisco for a few weeks to help to set up a system over there. Larry was a first-rate neurosurgeon and was clearly frustrated by activities that kept him away from plying his skills; activities such as walking

from one place to another. I had to get used to slipstreaming him to reduce the wind drag as we walked along the lengthy corridors of San Francisco General Hospital. I think I probably got more out of the visit than I put in. I did help a little and gave some lectures about our work in Glasgow, but I learned a great deal. Perhaps at the top of the *knowledge gained* list was an awareness of the differences between the UK and the USA in the role of medical physicists in health care and in research. There wasn't much of a career structure for us in the USA, and so when the issue of considering a move across the Atlantic came up, the answer was fairly simple, and I was saved from basketball and US politics.

The innovations coming from the Department of Neurosurgery are good examples of how research can have an impact on patient care. I've already mentioned the GCS. There was also the Glasgow Outcome Scale. The GOS was devised so that patients with brain injuries could be divided into groups to help to evaluate their recovery following different treatments. The outcomes were:

1. Death	Severe injury or death without recovery of consciousness
2. Persistent vegetative state	Severe damage with prolonged state of unresponsiveness and a lack of higher mental functions
3. Severe disability	Severe injury with permanent need for help with daily living
4. Moderate disability	No need for assistance in everyday life; employment is possible but may require special equipment.
5. Low disability	Light damage with minor neurological and psychological deficits.

Shortly after it had been developed the psychologists who specialised in measuring brain function felt that the five-point scale was too short as it lumped together patients who had quite significant differences in performance. The scale was expanded from five to eight points and became the Extended Glasgow Outcome Scale [EGOS]. The acronym was considered by some (unfairly) to be appropriate for a neurosurgical unit.

If asked to suggest factors that were critical to the success of this specialist Centre I would point to the multidisciplinary mix and the freedom to exploit this. When I started I knew nothing about the brain. I met with neurosurgeons over breakfast. We needed to top up our energy levels because I had run to work, and they had worked all night. I'd been reading scientific papers and books, but I needed the discussions to sort out all the knowledge in by brain. Throughout the day we met in canteens, coffee lounges and corridors. We had Wednesday morning research meetings that were open to all. It was just right: the right size and the right mix. It was a genuine global Centre of Excellence. It didn't use that title to describe itself. Others did.

The INS was one of several medical specialist Centres that were plugged into Health Boards. When I look back and think how lucky I was to have worked there, I don't think of the structure, or organisation. I think of the people; their character, expertise, and kindness. However, it was the structure that enabled specialist national centres of excellence to function effectively. The setting attracted high quality doctors and surgeons and gave them the facilities that they needed for the complex work that they undertook. This attracted visiting international experts and enabled worldwide partnerships to be established.

Financing Centres of Excellence

Perhaps the 1960s physical structure of the INS left a lot to be desired, but what about the organisational structure, and in particular the finance model used for these Centres? They were positioned within local Health Boards. As long as they shared facilities with the hospitals in which they were located, finance models were never going to be straightforward, and if they didn't share facilities then support services such as catering and laboratories wouldn't benefit from 'economies of scale'. So, should a specialist Centre have its own budget, coming directly from the central NHS pot, or should it be linked in with the host Health Board's allocation?

Many felt that it should have its own budget and that it should then pay the host hospital for services provided. That would have been the KISS option – Keep it Simple, Stupid. This option appeared straightforward, but of course a more convoluted system was devised. I remember having to take part in annual hospital equipment replacement meetings where resources for 'local' and 'regional' services were debated with no clear guidelines on how the money should be divided. This was a particularly critical issue because the main reasons for establishing regional Centres were, a) to generate a critical mass of clinical expertise and, b) to enable the necessary specialised equipment to be affordable. Having this equipment in every hospital made no sense. Surely that implied that the specialist Centre should have its own equipment budget, but it didn't. Equipment replacement funds for the general hospital and the INS were put in the same pot, with no clear guideline on how to apportion them. It was a strange setting. I felt that I had bought a ticket for the wrong concert.

However, the perennial equipment replacement problems shouldn't distract us from the excellent work that has been done at the Institute of Neurological Sciences, and is still being done. Recently I met a stroke survivor, who suffered a stroke ten years ago. He was admitted to the specialist stroke research unit within three hours and was one of the first patients to receive treatment with a pioneering clot-busting drug that is now commercially available. He went on to make a full recovery. Techniques are evolving to improve clinical management in many fields. They are being developed mainly in university hospitals like the INS and then taken on by other Centres and, if products have to be manufactured and distributed, by industry. The NHS is the test-bed for these developments, and streamlining the link between the NHS, universities and industry is crucial.

So, it's encouraging to see that hospitals are now being rebadged as 'University Hospitals' and that they have laboratory space for use by industry partners. This is good, but it's not a new concept. The development of CT at the EMI laboratories and the Atkinson Morley Hospital, or the development of medical ultrasound imaging by the University of Glasgow, the Hospital for Sick Children and Kelvin and Hughes Ltd shows that there were specialist NHS units that linked with universities and companies 50 years ago. Medical Physics Departments have always had strong links with industry. However, the 'new' University Hospitals, and the 'new' Innovation Centres, bring a new look, new funding, and new headlines. We have a constant urge to reorganise. More of the same is seldom good enough. In order to attract funding, we need new ideas. However, perhaps what we really need is simply re-cycling. Keep doing what has been shown to be effective, but freshen it up with a new name, a new façade, and hopefully new equipment. Reorganisation at its best.

Chapter 5: SPINNING the WHEELS of KNOWLEDGE

Medical Research

Research comes in many guises. You often hear the phrase, *I've researched it*. This can simply mean that the individual concerned has found out about something – read a book or looked up a dictionary, or now Wikipedia. In other words, they have increased their own knowledge. The research that I'm referring to aims to increase human understanding. Broadly it comes in two forms - research into the best way to do something using our existing knowledge, sometimes called health services research, and research to find new knowledge and understanding of the basis of medical disorders, often referred to as biomedical research.

Biomedical research is of interest to all around the world. Research findings come from all counties with the capacity to carry out the studies and are fed into the melting pot. They blend, and as a result progress is made. The contribution of each piece in the jigsaw can be hard to judge, as the jigsaw is invariably complex. Some pieces will turn out to be more important than others. Some will even turn out to be wrong. Despite peer review of publications, some studies have flaws and draw the wrong conclusions.

The good news is that we live in an age where there are scientific processes that can help to sort out the wheat from the chaff. The discipline of meta-analysis comes to our rescue. Meta-analysis is a way of sifting through published work on a topic to determine which findings appear to be replicated and which don't. As with most science now, statistical rigour is at the heart of this. To be included in a meta-analysis review, studies have to be of a sufficiently high quality. For example, the patients included in the study have to be clearly defined and meet the required criteria, and if there is an imaging component to the studies then this has to be of a sufficiently high quality. Meta-analysis helps to get around the problem that most studies are conducted on fairly small groups of subjects, sometimes because the specific condition being investigated is quite rare, or more commonly because of cost constraints. This is especially true of research involving medical imaging.

Another way of getting around the small numbers issue is referred to as 'big data'. In the case of medical imaging, 'image banks' are set up. Research groups from around the world can deposit images meeting the required criteria into a very large computer, or network of computers, and the combined dataset can be studied using statistically robust analysis techniques. By using this technique, the unintentional biases of small studies can be ironed out and so the results are more rigorous.

Research Conferences

Participation in local, national and international conferences is essential for good research. I'm referring here to conferences organised by learned bodies rather than those organised by pharmaceutical companies. They are far from being 'jollies'. Researchers work tirelessly to present their findings, listen to the finding of others and, importantly, meet with delegates from other centres to discuss the possibility of joint working.

Perhaps the main value to research teams is the deadline set by the conference. This applies in many walks of life, but especially in science as the urge to do further exploration is always there. The main deadline is normally set by the body funding the research, but having intermediate deadlines for analysis of data and presentation at conferences is helpful.

There is also the benefit of getting feedback from a broad range of experienced researchers. Keynote presentations by invited speakers at conferences generally reflect on work that has been completed and peer reviewed, but many of the general presentations by conference delegates will be on work that has been partially completed. '*Here are the results of what we've done, and here is what we intend to do next*'. This is the stage at which feedback is most valuable. The feedback might come from the questions that are allowed immediately after a presentation, but that is often show-time. The big

stage does lend itself to questions asked by delegates who want to show how smart they are, rather than genuine helpful suggestions. The best feedback comes in coffee lounges after the presentation, where groups can meet and discuss common areas of interest.

This leads to another benefit. Lasting partnerships, often with researchers from other countries, are invaluable. As with most professions, words creep into everyday use in research. One of these is the rather cumbersome 'generalisable'. This describes the extent to which research findings can be applied to settings other than those in which they were originally tested. Studies are more useful if they describe the true state of affairs outside their own setting. For example, a study of a specific treatment for clinical depression conducted on a group of patients in Edinburgh could be influenced by the method of recruiting patients and local socio-economic factors that affect these patients. If similar studies in Milan and Tokyo get comparable results, then the findings are strengthened. If they don't, then discussions on why this happens can be very helpful in identifying confounding factors.

All active researchers should take part in at least one international conference per year, and employers and funding bodies should support this. It is an essential part of the job. No matter how many research papers you read, you need face-to-face discussions to build up a full understanding of the issues that are being explored.

Conference participation does, however, have lighter moments. Here are a few light-hearted anecdotes.

Montreux, Switzerland: Travelling light

> One of my first conference escapades was with a colleague Alistair Jenkins, a neurosurgeon with outstanding talents. The first commercial MRI scanner in Scotland had been installed at the Institute of Neurological Sciences and Alistair and I had been involved in research led by Professor Graham Teasdale into the clinical benefits that MRI could bring to the management of head injured patients. Several of our group had papers accepted for presentation at a conference in Montreux in Switzerland. Transport to and from the meeting had been arranged by a Glasgow travel agent, and we were all set to go. At the eleventh hour we were contacted by the travel agent to say that there would be a surcharge to cover the transfer from Geneva airport to Montreux. Outraged, Alistair and I decided that the unscrupulous travel agent would not get a penny more, and that we would cycle the 95 km from Geneva to Montreux, which we duly did. As a novice cyclist at the time I had failed to take into account the problem that we would be arriving in the dark and I had no lights. This worked out well as I took Alistair's rear light and had to slipstream him for the final part of the journey.
>
> However, lights were not the only items that we shared. As we were cycling, and so travelling light, Alistair and I reckoned that one set of smart conference attire would be sufficient. Clever stuff. We are both tall and slim, so sharing made sense. However, what we found out when we arrived at the conference was alarming. We were down to give back-to-back talks. Perhaps this is the only conference in history where the speaker has handed the microphone and clothes to the next presenter. We decided not to swap trousers.

Padua, Northern Italy: The tour

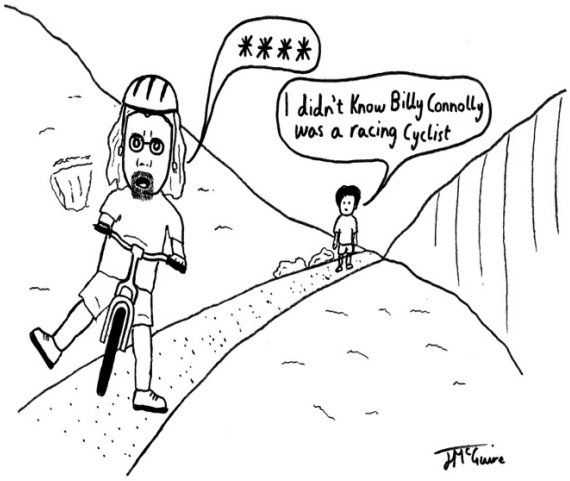
> Around 1992 I had been doing some research with psycho-geriatrician Derek Brown into Alzheimer's disease. One of the most important meetings that year was being organized by the Society for Cerebral Blood Flow and Metabolism and was due to take place in Padua in northern Italy. Derek was an avid cyclist and persuaded me that it would be a good idea to put our bicycles on the plane and cycle from the airport to the meeting. Then he gave the game away. He mentioned that if we took the long way home we could see a couple of stages of the Tour de France. The long way involved cycling across northern Italy to Milan, Turin and then over the border to Briancon in the French Alps.
>
> We hadn't done our homework very well and were unaware that bicycles could not be taken on express trains in Italy. We stood on the platform at Padua waiting for the express to Milan. The train arrived, and we boarded, lifting our bicycles up the steps and slightly annoyed that this was such a chore. The train didn't move. We sat for a while, unsure why so many Italians were gesticulating at us. Then two armed policemen approached. For a few moments we thought that acting dumb might work. However, this wasn't a US Presidential election, so that wasn't the best tactic. This was the Milan Train. Eventually an

American gentleman looked up from behind his newspaper and said, *"I think you guys should get off now"*. We did.

After a tortuous journey on three local trains we arrived at Milan. We'd had enough of trains. The next day we cycled from Milan to Turin. It's only around 80 miles as the crow flies, but the crow wasn't flying and the autostrade was no more appealing than intercity rail, so we meandered across the mosquito ridden plains of northern Italy. After three days we finally made it to Briancon, and the Tour. Our vantage point on day-one was at the foot of the climb up to Sestriere where Claudio Ciappucci had built up a sizeable lead. As he went flying past us he had a huge smile indicating that even at the foot of the final climb of the day he knew that he had won the stage.

Day two involved us climbing the Col du Galibier, a challenging 8,678 ft mountain pass. Although the physicist in me tells me that it makes no difference, 8,678 ft is much more impressive than 2,645 metres. Non-competing cyclists were allowed on to the climb as long as they arrived at the foot before the road was closed.

We danced our way to the Col, albeit with a foxtrot rather than a quickstep, stationed ourselves a few hundred feet from the summit and waited. Three riders had broken clear and the group included fellow Scot Robert Millar, as he was known in those days. As they passed nearby there was a collision, caused as often happens by a daft spectator who was high in more ways than one. Robert, who was not noted for his tolerance, made a few choice remarks. We didn't offer to interpret. Derek rushed to his aid and helped get him started with a friendly push. As soon as the race had passed we had a frantic descent to get back to our hotel in time to see Derek's assist on TV. So, as it turned out, Derek was the only conference presenter to get TV coverage that week.



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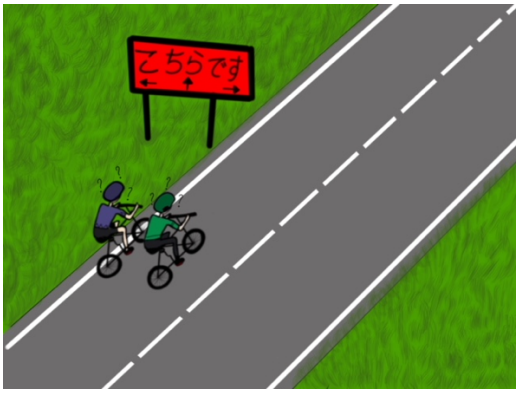
Sendai, Japan: Japanese hospitality

In 1993 I had a paper accepted for the Sixteenth International Symposium on Cerebral Blood Flow and Metabolism in Sendai, Japan. We were one of the few research units in the world that had the facilities and expertise to make a SPECT scanning tracer that could measure the loss of a type of brain receptor that had been shown in post mortem examinations to be affected in Alzheimer's Disease. Brain receptors were described earlier in the section on Positron Emission Tomography. The particular ones that we studied are involved in memory function. Drugs were being developed to help to preserve memory in Alzheimer's and our preliminary results suggested that they would not work in patients with advanced disease as there were too few receptors left to work on. This wasn't a radical breakthrough, but it helped to add scientific evidence to what was being observed in clinical practice.

As often happened, transport to the conference became an issue. Again, Alistair was the culprit. The plan was to put bicycles on the plane and cycle the 304 km from Tokyo to Sendai. On arrival in Japan we were told by KLM that the bicycles were still at Newcastle. We were, however, reunited with our bicycles in time to cycle back from Sendai to Tokyo. This was not as easy as we had anticipated. We had made the mistake of buying maps in the UK before leaving. Strangely, on the small cycle-friendly roads in Japan they don't have signs in English. Several times we were totally lost, but help was never far away.



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One day it was starting to get dark and we hadn't a clue where the nearest town was. We came to a rural shopping mall and stopped to ask directions. We approached a middle-aged couple and a young teenage lad was ushered over to act as interpreter. They then gestured to us to follow their car and guided us for 12 km, not just to the nearest town, but to the hotel doors. It was a small village and the hotel owners treated us like royalty. I had taken my practice chanter and gave a short recital. Well I couldn't take a full set of bagpipes on a bicycle. Our hosts responded by showering us with gifts, including paintings that are still on display in our homes. The hospitality was second to none.

The icing on the cake was when we set out to cycle south after the conference had finished and had covered about 20 kilometres when Alistair discovered that one of his panniers had broken off. Unfortunately, this must have happened on one of the rare occasions when I was in the lead and so it went unnoticed. We stopped and retraced our steps or peddles, but all to no avail. Alistair was very upset at losing his best suit, although quite why I'll never know. However, as it turned out, he didn't lose it. A couple in a passing car had seen the pannier flying into the ditch, stopped to retrieve it, and then waited at the next lay-by until we came along. As we had retraced our steps this took a couple of hours. Would anyone do that here? If it hadn't been for the combination of cycling and our ineptitude, I don't think we would have experienced the incredible warmth and friendliness of the people in rural settings in Japan.

Valamo, Finland: Dress Sense

At the time when our research team in neurosurgery was developing ways of measuring brain blood flow, a group in Finland was engaged in similar work. We had published some results and I was invited to a meeting of the Finnish Nuclear Medicine Society to present them and discuss them with the local scientists. The meeting was held at the Valamo Monastery in Finland. This has a long history, dating back to 1717, but the current monastery was established by the Finnish Orthodox Church in 1940. In keeping with tradition, it has to be fully self-sufficient. Reorganisation here has been extremely beneficial, as the original strategy of tilling the soil has been replaced by setting up a distillery and by encouraging tourism, including hosting conferences.

I knew in advance that the conference would conclude with a formal dinner and having viewed pictures of the previous event I thought that it would be appropriate to take my kilt and Prince Charlie jacket. When I saw the local delegates arriving in their splendid national costumes I was glad that I'd done this. As I arrived for the dinner I met John, a colleague from the USA. I was quite familiar with his work and so we engaged in conversation as we approached the venue. We were met by the host and his wife, resplendent in very colourful outfits. He greeted me warmly and said how nice it was that I was wearing my national costume. He then turned to John, in his jeans, T-shirt, and trainers, and said *"And it's good that you are wearing yours".* America did give us jazz, but not rock and roll (that was God), and they are maybe not world leaders in national dress.

Glasgow, Scotland: Scaling the heights

Those given the responsibility of marketing Glasgow launched a new slogan in 2013, "People Make Glasgow". The 2014 Commonwealth Games held here branded Glasgow as the "Friendly City". I'm sure it is, but I do prefer it when others tell you how friendly you are, rather than you bragging about it. My experience has been that Glaswegians are on the whole very hospitable, but that could be applied to many cities. The need for contrast was discussed in the imaging sections above, and perhaps it's the proximity to Edinburgh that brings out the contrast that gives Glasgow the 'friendly' label.

In 2008 I went with Sally, a colleague who specialises in radio-chemistry, to a meeting in Pittsburgh. The title of the event was NRM2008, NRM standing for Neuro-Receptor Mapping. These meetings are held every two years, and unlike most conferences they are not underwritten by a learned society. Those taking part are very specialised, working to develop new tracers for PET and SPECT. At each meeting delegates who would like to host the next meeting make a pitch to the audience and then a vote decides on the winner. In a moment of madness a few months earlier Sally and I had decided, along with a third colleague Jonathan, who is also a specialist in radio-chemistry, that we would make a bid. Hosting meetings like this is very good for the local economy as participants have to stay in hotels, eat in restaurants, hire taxis, and buy gifts. They often stay on for an extended break after the main event and

bring other family members. Even a small three-day meeting like ours with just over three hundred delegates can add well over a quarter of a million pounds to the local economy.

I had to prepare a 'Come to Glasgow' pitch and was helped enormously by the Glasgow Ambassadors Organisation who had a stunning promotional video. We were up against groups from Manchester and Vienna. Each group was capable of hosting the meeting with good conference facilities, so it boiled down to the extras on offer. Manchester could offer a tour of a football stadium and Vienna had the stunning backdrop of the Alps. We couldn't match this backdrop, and so I threw in a promise that the three hosts would personally escort any delegates who wanted to participate in a climb to the highest point on our less impressive, but easily accessible, backdrop. As soon as the meeting finished we would lead a party to the summit of Ben Lomond.

Voting had never been tighter. We won by getting one vote more than Vienna and two votes more than Manchester. So NRM 2010 was coming to Glasgow. In case one of the delegates had cast their vote on account of the promise of a hill-climb we felt obliged to honour the commitment. For obvious liability issues, we were careful to badge the climb as unofficial and voluntary. We were certainly somewhat anxious when we thought about what could go wrong, but of course those who took part were self-selecting and managed the 3,200 feet with no bother. In fact, it proved to be a good way to unwind after the hard work of the conference and was an opportunity to get more acquainted with some of the visitors. Perhaps international meetings of politicians should include activities like this.

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What does an R&D Director do?

Bureaucracy defends the status quo long after it has lost its status.

Laurence J Peter

One of the frustrations of medical research is that it can be a very bureaucratic process. Quite rightly ethics approval is required before a research project can start. In general, this is handled very well within our NHS. It is a relatively speedy process. I have never personally experienced a situation where a project was refused ethics approval, and I don't recall encountering any colleagues who had. Researchers know the guidelines and as long as they are adhered to there should be no major problems. Ethics committees sometimes suggest modifications, but these are generally aimed at improving the project rather than preventing it from going ahead. For example, they might feel that too much of a demand would be placed on the patients who volunteer for a study and recommend some simplifications. This generally leads to a better, more focused, study. Researchers can be overenthusiastic at times and want to solve too many problems at once.

There are, however, other hurdles that researchers have to clear. Approval might be needed to store and retrieve data from computer systems, and what is referred to as R&D Management approval is required. R&D Management didn't exist when I first started but came into the NHS along with many other management systems. Why should research escape the net? R&D Management is now a profession. There are R&D Management Conferences where the management process rather than the research is discussed. Hospitals have R&D Directors, R&D Managers and R&D officers. Their role is to ensure that all the paperwork is in place before a study starts and that all the reporting is undertaken. In theory this should help researchers, and although it can be overelaborate, it generally adds value.

I drifted into the role of R&D Director without much forethought. It was never intended to occupy more than a few hours each week. A couple of clinicians had tried to fill the role before me but found that their patient commitments made it difficult. The timetables of most clinical scientists were a bit more flexible and so I was asked to have a go. I didn't particularly enjoy doing this, but I did find it very interesting and it brought me closer to the processes involved in funding medical research; in particular the bureaucratic processes introduced by civil servants within central government offices. After going through the initial learning phase, I set out on a crusade to improve the processes and reduce the bureaucracy. I failed.

One of my tasks as R&D Director was to make the case for our hospital's R&D support income. The purpose behind this was to account for the fact that general hospitals contributed very little to research whereas teaching hospitals incurred a significant overhead caused by this additional work. So, their income from central government should reflect this. Complex ways of determining the extra income were set up – a bit like many of our complex taxation systems. I'll not bore you with the details. Suffice it to say that my fellow R&D Directors and I knew that the system that was in place was rubbish. It was totally artificial and was not an accurate reflection of the quality of research that was taking place in hospitals. It remained in place for many years until it was eventually replaced by a better process, although this was still far too complex. It shouldn't have taken so long for the bureaucrats to address this.

Intellectual Property

Another challenge that faced us in the R&D Office was to develop an Intellectual Property [IP] policy for the Hospital. Universities had these, but this was new ground for hospitals. Fortunately, a few hospitals in England were ahead of us and so Susie, our excellent R&D Manager, was able to replace a few words in one of their policy documents so that we could present 'The South Glasgow NHS IP Policy' to our Board for approval. Such was the importance attached to it that it took several Board

meetings before space was found on the agenda. The Board members were clearly not excited about this, and frankly I don't blame them.

IP protection prevents an individual or a company from stealing other people's ideas. It was set up to stop copying. Inevitably this can get very complicated. How much modification is required before you have a new idea rather than a copy of an existing one? Clearly there was a need for judgement, and so judges and lawyers. A whole profession of Intellectual Property law was established.

When companies or public organisations establish an IP policy, sometimes the first section of the policy that employees read is on the distribution of royalties. What do I get out of it? At the time of the Penject project that I mentioned earlier there was no process for rewarding inventors. All the proceeds went to the Health Board. Later, however, the rights of employees crept in and a proportion of the income went to them. In commercial companies this was a modest percentage, but for some reason in public organisations like universities and health boards it was a much larger percentage. We ended up with 50% going to the Health Board, 25% going to the inventors and 25% to a research fund controlled by the inventors. This meant that the various inventors in a team had to agree on their relative contributions. As R&D Director I did hear some mumblings from time to time, but we never had a formal dispute that had to be resolved, although we did have a process for that if it had been required.

The closest that I came to having a dispute to settle concerned a project to develop a safe hinge for doors. It had been noticed that there were quite frequent injuries to young children because their fingers had been trapped at the hinge side of a door as it closed. These could be nasty injuries. A couple of young students from the School of Art were presented with this challenge and came up with a very effective redesign that prevented these injuries. The product was marketed. However, one of the doctors who had put the challenge to the students claimed that he should have a sizeable share of the IP income. He threatened us with legal action. We ignored this and carried on. You don't own any IP by bringing a problem to the table. You own it by contributing to the solution. It was fairly clear that he didn't even understand the new designs, far less having contributed any ideas. He must have received good advice from his lawyer, because the problem disappeared. The project was a great success and went on to be central to the formation of a start-up company, Safehinge. Now, twelve years later, it is going from strength to strength.

I never felt completely comfortable with individuals in the NHS or Universities being rewarded for their contributions to IP. By the nature of their work, some employees have more opportunity than others to work on developments. Rewarding people for doing their job well has already been discussed, examples being a doctor receiving a merit award, or a banker receiving a bonus because he meets targets. All of this happens, and it troubles me. We should all do our jobs to the best of our ability. If the outcomes are good we should take pride and satisfaction from that, but not extra money for doing what we ought to be doing. I really liked the component of our IP policy that awarded 25% to the **research fund** of the inventors. This helped them to keep up the good work. Their proven success was used to reduce their grant-writing burden and left them with more time for further research and development. I wish it had been 100%.

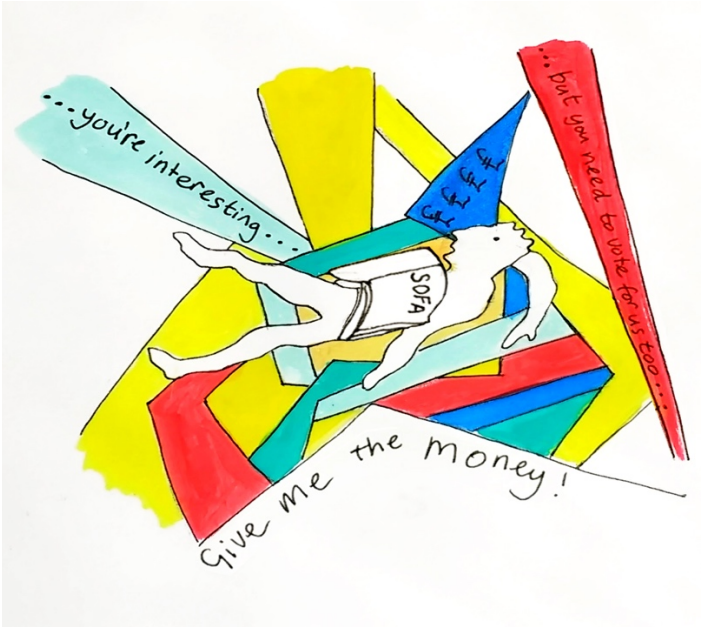
The other problem I have with individual ownership of intellectual property is that I'm not sure that it is a true reflection of the processes involved in innovation. We don't dream up brilliant development ideas in a vacuum. Many of the best ideas start out as very bad ones, but you present your ideas to colleagues, they are bounced around, modified, revised, bounced around again, and so on until better solutions emerge. The wider the group discussing the ideas the more informed the solution. The concept of IP can lead to secrecy and to narrowing down the group of colleagues. I can understand the need for IP rules at organisational level to protect companies, but I struggle when it comes to monetary reward for individual contributions. I gather that top-flight profession footballers now get a bonus for scoring a goal and even for what is called assisting, the player who sets up the goal. What a ridiculous concept in a team game. Technology development is a team game as well. By all means have a winner's bonus, but give it to the whole team, and the best way to do that would be to put all the income in their research fund. Having spent 47 years working with medical researchers, I get a strong feeling that most would support this.

Where does the money come from?

As I mentioned in the introduction, the hope that this short book might bring in some funding for medical research was one of the reasons for writing it. I've been involved in the funding cycle for many years, both as an applicant, and more recently as a reviewer of grant applications. Research funding organisations rely on the good will of scientists who peer review applications. As with many other skills, I was never taught how to review. I don't think many scientists are. You pick it up, and hopefully for the benefit of researchers you pick it up quite quickly. Most researchers are called on to peer review research grant application. Why do we do it? You're not paid to review. Perhaps there are two main answers. Firstly, curiosity - the curiosity that leads you into research in the first place. Secondly, a sense of duty. Someone has to do it, and perhaps driven by conceit, you feel that you are that person.

A problem with the peer review system is the length of time that the process takes. If you are applying to one of the major UK or EU funding councils, you have to plan well ahead, as it could be up to a year between submitting an application and starting the project, assuming of course that you are one of the 20% or so who end up being successful. When you sit back and think about it, the whole grant funding system is bizarre. It is flawed through and through, but perhaps like democracy, it's the best that we can come up with. It has always struck me as ironical that research scientists are supposed to be bright, and yet they have failed to come up with a better system. It has been estimated that a grant award of £40,000 has cost around £10,000 to procure if you factor in the time spent by the applicants and the cost of review, which as I've mentioned is relatively small as it is mostly pro-bono. And perhaps more importantly, is the sluggish time cycle appropriate in such a rapidly developing field? Do we have good processes in place to distribute research funding? Is it good that it often takes so long?

Many researchers acknowledge the shortcomings, but we have failed collectively to come up with a better system. There is an interesting proposal that is getting some publicity just now called SOFA: Self-Organized Fund Allocation. Using this system, researchers would no longer have to apply for grants. The national pot of money would be distributed to all research groups with the proviso that they have to donate a fixed percentage, say 50%, to other groups, and they must not have any association with these groups. That would mean that groups with most respect amongst their peers would get most money, which is exactly what the current system sets out to do. However, SOFA would have a very small overhead and fewer delays.



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There are several tiers of research funding. We have small local pilot studies, larger national studies, multi-national studies and mega studies that need massive pieces of equipment. Where could SOFA fit in? Initially it would probably be at national level, but we would have to do something that politicians generally have difficulty with. Take it a step at a time. It might take more than a single term in office to set it up.

There would have to be rules. We would have to conduct pilot studies. Groups would have to register, and regulatory statistical frameworks developed. These would have to be trialed in a few settings. This would be best done in medium sized countries where it could be managed and yet lead to sufficient funding for good groups to undertake studies that would make a valuable impact. Countries like France, Germany or the UK would be ideal. It is being discussed in the Netherlands, and a pilot

study there could certainly help to iron out some of the teething issues. What is needed is something that scientists are generally not very good at. We need to persuade politicians to be brave and experiment with a new system that could reduce bureaucratic overheads and yet still lead to high quality research, with the best groups getting most funding support. It wouldn't be high risk, because the money would still go to research. In the long term, more money would go to research. It would take time to reduce the number of bureaucrats in the system, but that would be OK. We'd be patient. But this is only a dream. Would the powerbrokers and civil servants within the funding councils ever allow it to happen? Turkeys and Christmas!

The Neurosciences Foundation: NSF

In addition to the large national funding bodies such as the Medical Research Council [MRC] or the Engineering and Physical Science Research Council [EPSRC] there are major and minor charities. The major ones like Cancer Research UK or the British Heart Foundation function along similar lines to national funding councils, but the money comes from charitable donations and legacies rather than from taxes. Then there are many small charities. I am involved with one of these, the NeuroSciences Foundation - NSF. This was originally set up in Glasgow in 1978 as the Institute of Neurological Sciences Research Trust with the objective of providing small grants to help junior researchers to establish research careers or to help research teams to get preliminary measurements that make funding applications to a major funding body more plausible.

If, for example, researchers were to apply to the MRC for £400,000 to investigate the value of a novel imaging technique in stroke, and it was all just a theoretical idea, they probably wouldn't be successful. If, however, they were to get £10,000 from the NSF they could conduct a small pilot study. The findings from this would enable them to present some initial results to support their bid for a £400,000 grant for a more complete study to improve the technique and apply it to a larger group of patients. Reviewers would have confidence in their ability to undertake the study and so funding from the MRC would be more likely. The good news is that this is actually happening. One study recently supported by the NSF led to a £700K MRC grant and another one to an EU Grant Award of 600K Euros as part of the EU ERA-NET-NEURON programme.

Over the years the NSF has provided over one million pounds to support a wide range of projects. Here are some examples of the work that's going on in **brain cancer, stroke** and **head injury.**

1. **Oncolytic Viruses – Viruses Designed to Kill Cancer Cells.**

   See also - www.virttu.com. After a special fund-raising campaign a larger than usual grant was awarded to researchers investigating the potential of a modified virus to attack cancerous cells in brain tumours. The virus, HSV1716, is similar to the one causing cold sores, but has been genetically modified so that it replicates only within rapidly dividing cells. It had been shown that cancer cells in test-tubes were killed by HSV1716, but normal cells weren't. The virus particles simply kept growing inside the tumour cells until they burst.

   The research was led by Professor Moira Brown, a virologist at the University of Glasgow. Preliminary results were extremely encouraging, and a spin-out company called Crusade Laboratories was set up with support from a private Jersey-based investor. As often happens in clinical research many barriers have been encountered in converting the finding in a test-tube into an effective therapy for humans. The main problem has proved to be in getting the virus particles into tumours in sufficient quantities to be effective. This has not yet been successful in clinical practice, but the quest is still underway. Crusade Laboratories morphed into Virtuu Biologics and further progress is being made. As a rule, big medical breakthroughs don't happen overnight.

2. **MRI in Stroke**

   See also - www.aurumbiosciences.com. This study was led by neuro-radiologist Dr Celestine Santosh who works at the Institute of Neurological Sciences in Glasgow. Tosh, as he is affectionately known, came up with the brilliant idea of modifying the BOLD [Blood Oxygen Level Dependent] process described in the MRI section. Images need something that will provide

contrast between one region and another. With fMRI, the signals that are detected using the BOLD pulse sequence are used to distinguish regions of the brain that are active during a certain task from those that are less active. These regions end up with more oxygen and that provides the MRI contrast as it alters the nuclear spin.

Tosh and his colleagues developed the GOLD [Glasgow Oxygen Level Dependent] pulse sequence. To apply this technique the level of oxygen in the whole bloodstream has to be varied. This change has a different effect in healthy brain tissue compared to less healthy tissue that isn't able to work well enough to use up the oxygen. Instead of depending on which parts of the brain are involved in the performance of a task, as happens in with fMRI, the images produced using the GOLD technique depend on how healthy the different parts of the brain are.

The main use is in assessing patients after a stroke to determine how much brain tissue has been unaffected by the blood clot; how much is dead, and how much is 'at risk' and might survive with good treatment. As with the viral therapy research mentioned in the previous section, this team also set up a spinout company, called Aurum Biosciences, after their acronym GOLD.

There is an interesting and unusual aspect to the early work to develop the GOLD MRI technique. It had been shown to work in patients before any animal-model studies were undertaken. It is common to test ideas in an experimental setting and then try to translate the science so that it works in a clinical setting. This is called translational medical research. However, to try out the GOLD technique in patients was fairly easy. Neuro-radiologists just had to alter blood oxygenation in patients who were being ventilated and also being scanned using MRI, and by doing this it became apparent that healthy brain responded differently to unhealthy brain if oxygen levels were changed. A few rodent studies were still required however, in order to make measurements in a very controlled setting and learn much more about the various factors that could influence BOLD contrast. So, this was inverse translational research. The researchers started out knowing that they could get an MRI contrast between healthy and unhealthy brain but didn't know precisely what factors affected this. They had then to undertake studies in a more controlled setting to gain a better understanding of what was happening before going back to do more focused clinical studies.

The GOLD story doesn't end here, however. For many years radiologists had been seen as purveyors of bad news. They could tell you what was wrong. A negative scan with no abnormalities was dull, whereas they could delight in their ability to detect abnormalities. *'Gather round while I show you this fascinating infiltrating astrocytoma'*. Fascinating for the radiologist but devastating for the patient. Then along came interventional radiology. Instead of having to cut the body open to repair narrowing blood vessels, techniques were developed to enable radiologists to insert tools to remove the debris and then poke what are called stents along the blood vessels to the faulty part and expand them to provide a strong lining. This can be applied to blood vessels feeding the brain or the heart. So, radiology moved from being purely for diagnosis to being of direct value in patient treatment.

And so it is with GOLD. For this technique to work, there has to be a way of altering the amount of oxygen in the blood. This can be done by injecting a material called a perfluorocarbon, or PFC. The particular PFC used by Aurum is ABL101. In addition to altering the blood oxygen concentration levels to provide a contrast to the MRI signal, PFCs are being evaluated clinically as a way to increase tissue oxygenation. In other words, if the current clinical trials of ABL101 are successful, the technique might not only help to identify how healthy the brain tissue is in the regions affected by a stroke, but it might also help to reduce the damage by improving oxygen delivery to parts that normal blood can't reach. PFC molecules are forty times smaller than blood corpuscles and so are less affected by the blockage in the artery that caused the stroke.

Clinical trials are currently underway. In order to finance these $4.5M had to be raised by Aurum. If the trials are successful, then the small award of around £10,000 from the NSF will have gone a long way. A stroke is a devastating event. There are around 150,000 instances of stroke every year in the UK alone and over 1.2 million stroke survivors. The potential benefits from this research to the quality of life of those falling victim to a stroke are enormous.

3. Intensive Care Monitoring: The Brain-IT Project

See also - www.brain-it.eu. A patient with a severe head injury would generally go to a neurological intensive care unit. In many of these, recordings would be made of the pressure in the

brain – intracranial pressure or ICP. There are various ways of doing this. A tube can be inserted into a fluid compartment near the centre of the brain, or more commonly a pressure-sensing device can be inserted just under the skull. As well as measuring the pressure in the brain, these devices will show how this varies with time, typically making many recordings per second. In this way, an ICP waveform is produced.

If the intracranial pressure gets too high this is clearly bad. The high pressure acts against the pumping of the heart and it becomes more difficult for it to deliver enough blood to the brain. But is there any additional information in the shape of the ICP waveform? Doctors can tell a lot about what's going on in the chest by listening to sound waveforms using a stethoscope, and it may well be that the ICP pressure waveforms might alert us to abnormal events within the brain.

However, a major problem facing doctors and scientists who were conducting research into this was that each group was using different processes. It was all a bit of a mess. The team that received funding from the NSF was led by Dr Ian Piper, a medical physicist in Glasgow. Ian saw that what had to be done initially was to bring the various groups from around Europe together so that they could set up standard processes and thereby build up data-sets that were sufficiently robust to produce results that are statistically valid. With pilot data gathered in a project supported by the NSF he applied to the EU and has now had three successful grant applications to help to set up the required infrastructure and most recently to conduct studies to predict when all is not well with a patient so that preventative action can be taken in time. Researchers from 22 cities across 11 countries in Europe have joined the group. They are now collecting data using common protocols and feeding this into a central computer for analysis.

Like many projects this is not research that has so far found its way into clinical practice, but we are realistic and know that medical science seldom has quick fixes. It's also worth pointing out that the very existence of the group is beneficial. Members meet regularly to discuss their work. We shouldn't underestimate the value of a discussion that ends with '*we've tried that, and it didn't work*'. We can all learn from each other, and the wider the circle of contacts the better.

Neurosciences Foundation Studentships

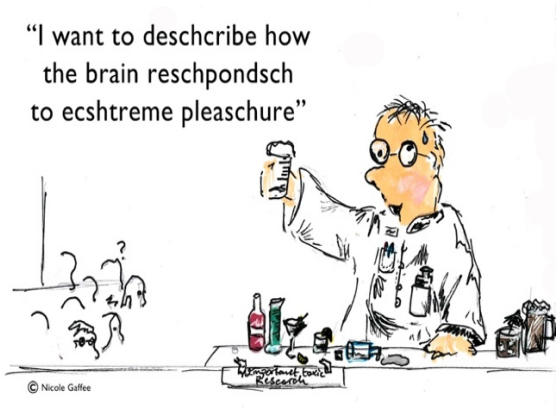
Studentships fulfill two objectives. The students help to advance knowledge by working on projects within well-established teams and at the same time they learn from some of the best researchers. By 2014 the Neurosciences Foundation had been in existence for 36 years, but it had never supported the employment of people. It provided funds to buy equipment or to access equipment that had already been bought. However, what most researchers really want more than anything else is an extra pair of hands, in particular when the hands belong to someone who is bright, enthusiastic and keen to learn.

Acknowledging this, the Trustees agreed to set up the NSF studentship scheme. This was a bold venture for the Foundation as it involved a larger commitment of funds than we were accustomed to. In order to ensure that the studentship can go ahead our funding is conditional on matched funding being found from another organisation. One reason for this is to make it affordable, but it is also important to know that another funding body will buy into the project. So far, we have funded three studentships, with matched funding coming from other grant awarding bodies or, in one case, from industry. As I write this we are about to award a further two studentships. Here are brief summaries of the first three:

The Multiple Sclerosis project. Two of our students are working to develop tracers for use with PET. Tim is our first student. He is being supervised by Dr Andrew Sutherland, an organic chemist who has the skills necessary to develop these tracers. Tim is producing novel chemical compounds that could be used to assess drugs that are being developed to treat patients with multiple sclerosis. Faults develop in particular molecular processes in the body and this leads to MS. Drugs could counteract this, but we need to be able to see whether or not they are doing so. Just waiting to see if the symptoms improve isn't good enough. This would take time and other factors could affect symptoms. We need direct measurements of drug action. PET could do that if appropriate tracers can be developed. Tim is making good progress. We were delighted to see that he has made a YouTube presentation describing his work.

The Brain Tumour project.

Maria is our second student. She is being supervised by Dr Sally Pimlott, whose expertise is in radiochemistry – the production of tracers. Her project is similar to Tim's but the target is very different. The aim is to develop PET tracers to study glioma, an aggressive form of brain cancer. Maria has also made a YouTube presentation. Encouragingly, Maria is passionate about the need to communicate science to non-specialists and helped to organize one of the 2017 Pint of Science events in Glasgow. Speakers are challenged to describe their research in 15 minutes and to entertain.



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The Parkinson's Disease project.

Callum is our third student. He is working with Dr Donald Grosset who is an expert in Parkinson's Disease. Some PD patients develop dementia, and one of the big challenges for doctors is to determine whether the dementia is due to PD or is another type, such as Alzheimer's Disease. Tim will have access to a large dataset from a national UK study on PD. He will sift through that to look for patterns that might help to characterise the dementia. The research team will then conduct a prospective study to test the findings on a group of patients in the west of Scotland.

I hope that we are able to support many more studentships. We are investing in our future.

Fundraising

Originally all of the money donated to the Neurosciences Foundation, apart from the inevitable fees paid to auditors, was used to support research projects. Recently however a small percentage has been used to employ a fund-raiser. This has been cost effective, but fundraising is still a struggle for small charities like ours, especially when the general economy is in decline. If a philanthropist would step up to the mark that would be wonderful. In the USA this might be realistic but in Scotland it is more challenging. We live in hope however.

The author JK Rowling has donated generously to the University of Edinburgh to support Multiple Sclerosis research and there are many other potential backers out there. Sadly, many choose to support political movements that, by definition, are parochial, rather than medical research groups, that aim to improve the quality of life of us all.

The Sackler Foundation.

The next step for researchers who get encouraging pilot data from studies supported by small charities like the Neurosciences Foundation is to apply for larger grants. They have two options; government funding councils or large charities. In 2004 one of the research groups that I was working with was successful in a bid made to such a charity; the Dr Mortimer and Theresa Sackler Foundation. The aim was to fund research into psychiatric disorders. A condition attached to the

award was that the researchers at the University of Glasgow had to undertake collaborative studies with colleagues at the University of Edinburgh. The Glasgow group led on clinical depression and the Edinburgh group on schizophrenia. Research into each of these conditions aims to improve our understanding of chemical pathways and connecting circuitry in the brain, and so the collaboration broadened the range of expertise.

Mortimer Sackler (1916 – 2010) was the son of a Polish Jewish immigrant to the USA. He attended high school in Brooklyn but failed to get a Jewish-allocated place at medical school in New York and sailed to the UK in 1937. He was integrated into the Glasgow Jewish community and was able to enroll at the Glasgow University College of Medicine. Although World War 2 began before he could finish his studies he was later able to complete his degree at the Middlesex Hospital School in London. It was the University system in Scotland that launched his medical career and he didn't forget that.

Along with his brother Raymond, Mortimer set up a pharmaceutical company that marketed an opioid-based painkiller. Possibly there was a degree of spin in the marketing of this, but it set up a family fortune that has led to philanthropy on a very large scale.

The Mortimer and Theresa Sackler Foundation has been invaluable to both medical research and the arts. In addition to many Medical Research Centres, they set up the Sackler Wing at the Metropolitan Museum of Art in New York and the Sackler Biodiversity Imaging Laboratory at the Natural History Museum in London. Both are well worth a visit.

Visiting the Temple of Dendur at the New York Met is a very special experience

At the formal opening of the Glasgow Sackler Institute I sat beside Theresa at lunch. I was aware that her background was in nursing and thought that she might be interested in a major development that was taking place in the NHS. A new grading scale for clinical support staff had recently been unveiled. It was called *Agenda for Change*; yet another example of reorganisation, although in this case one that made considerable sense. The objective was to harmonise the pay scales and career progression of all NHS professional staff with the exception of doctors, dentists and senior managers. Countless hours were spent by each employee working with their line manager to develop a new job description for their post and making sure that it included key words and phrases that would ensure assignment to the highest possible point on the grading scale. The harmonisation process took many years to complete. I set about explaining what was going on to Theresa. She listened intently, but with a slightly quizzical look. After a while she sat back and exclaimed; *"Ah, Agenda for Change. I thought you were talking about gender change!"* Maybe that would have been much more entertaining.

The support from the Mortimer and Teresa Sackler Foundation proved to be invaluable and helped both Glasgow and Edinburgh researchers to advance their research programmes and win further awards from major funding bodies.

SINAPSE: The Scottish Imaging Network; a Platform for Scientific Excellence.

Alone we can do so little; together we can do so much.

Helen Keller

I've stressed how important collaboration is in medical research, so it might be appropriate to end this chapter with a look at a splendid example of that.

In 2007 the Scottish Funding Council [SFC] agreed to provide £7.3M over 5 years to set up SINAPSE, one condition being that the Universities involved in the partnership had to ring-fence a tiny proportion of their general allocations to support this. Several such groups were set up, most with catchy acronyms. So SUPA was the Scottish Universities Physics Alliance; SULSA the Scottish Universities Life Sciences Alliance; SICSA the Scottish Informatics and Computer Science Alliance; MASTS, the Marine Alliance for Science and Technology for Scotland; and so on. The idea was to form groups that could pool the best expertise and facilities from several Universities so that stronger partnerships could be formed. SINAPSE was originally a group of scientists and doctors from the Universities of Aberdeen, Dundee, Edinburgh, Glasgow, Saint Andrews and Stirling. Recently the University of Strathclyde recognised the benefits and bought into the consortium, so now seven institutions are members. It is unique amongst the pooling groups in that it also receives funding from the NHS in Scotland. The theme is medical imaging, and so it is a group of academic experts who use the technologies that have been the theme of this book. Most of these experts work in hospitals, but the imaging technologies are also used by psychologists to study brain function, and they are valuable members of the SINAPSE network.

The hard work in persuading the Funding Council to part with £7.3M was led by Professor Joanna Wardlaw, a neuro-radiologist at the University of Edinburgh. Representatives from each of the participating universities were assembled in Edinburgh to face a review panel. At the end of the interview it was agreed that a pooling group in medical imaging would be set-up, but only on condition that we modified our bid. We had asked for 12 PhD studentships, but were told that a condition of the award would be that we had to accept 24 studentships. It was the first time I had ever known a review panel to argue for an increase. They weren't daft of course. The funding council paid for only half of the studentship and so this was a way of getting a larger commitment from the Universities, who had to pay the other half. Fortunately, they bought into it. I was delighted at this as I've always been passionate about the value of studentships. It is education at its best and a huge boost for research teams.

At that stage the group didn't have a name and one of our first challenges was to come up with one. The simplest and punchiest would have been SIN, the Scottish Imaging Network, however we added the APSE to make it more acceptable. SINAPSE, with an 'I' and not a 'Y' was a good choice, although it did understandably lead to the belief that it is a brain imaging network, whereas in fact it covers imaging techniques used to study all parts of the body. The NHS provided additional funding to pay the initial salaries of two Professors of 'non-brain' imaging to ensure that this happened

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For the first few years of SINAPSE I was involved as one of the Executive members, representing the University of Glasgow. Glasgow was unique amongst the Universities in Scotland in that for some bizarre reason it did not [and still does not] have an academic radiology department. So, the closest they could get was Clinical Physics. During the first few years of its existence I really warmed to the concept of academic partnerships. At the beginning I had wondered if it would work. Universities are set up to compete. Their income from the Government depends on how they perform in relation to each other. Would this be like suggesting that Manchester United and Manchester City should form one team? Of course it wouldn't. It would be like selecting players from each club to represent the national team. A sufficient number of SINAPSE members recognised that the whole could be greater than the sum of the parts, with the result that medical imaging in Scotland has become more competitive internationally.

The studentships were a great success. We ended up with 45 rather than 24 as further funding opportunities appeared. The quality of graduates who applied was outstanding, and there was a healthy blend of nationalities with around half coming from the UK and others from further afield. Perhaps one of the attractions was that the students recognised that they would be part of a national network and so have access to the best researchers in Scotland. The gender balance within our group of students was interesting – 23 male and 22 female. Gender balance is, quite rightly, a topic of much interest in science. At no point in our recruitment processes was gender an issue. We gave no consideration whatsoever to country of origin, beliefs, or gender. Our selections were based on scientific knowledge and personality. We were open-minded, and, importantly, had no constraints. This worked well. The students were fantastic, and the multicultural element added significantly to the dynamics of the group. The SINAPSE annual three-day student induction events were particularly memorable. They covered scientific thinking, scientific presentation, and of course our local culture, ceilidh dancing. This was so far away from the xenophobic thinking that is sadly appearing in many settings. It is even more rewarding now, as several of the home grown and also several of the international students, have gone on to deploy their talents in more senior posts around Scotland.

I'm sure this applies in many settings, but the achievements of SINAPSE are due in no small part to the skills of the programme managers – in our case firstly Janet and now Kristin. Directors help to create the setting and the scientists who undertake the day-to-day activities make it work. You can follow the progress of SINAPSE on www.sinapse.ac.uk.

As with most networks, many of the achievements don't lend themselves to outcome assessment by precise criteria as it's possible that they would have happened without the additional input from the network. We provide extra hands and additional academic input to dozens of research programmes that are being led by one or more of the partner institutions. This is extremely valuable but is hard to quantify. However, some outcomes are very clearly down to the work of SINAPSE. For example, we hosted several events that would not otherwise have taken place.

A splendid example of this is the workshop on *Brain Imaging and its Impact on Society,* which was held in 2010 in collaboration with the Institute for Advanced Studies based at the University of Strathclyde. Taking part were lawyers, judges, philosophers, political scientists, church representatives, sociologists, neuroradiologists, neurologists, neuroscientists, psychologists and bioethicists. Several topics of general relevance were debated, including the use of scans for marketing, for recruitment of staff, or for legal purposes. There are businesses in North America offering MRI scans to classify those who are more likely to tell the truth or those more likely to tell a lie.

The scientific debate that needs to take place here is not so much about the scanning processes, but about statistics. It's down to likelihoods; to the specific personal physiology of each individual. There might have been studies that show a statistically significant difference between a hundred truthful people and a hundred liars, but where do you fit into this? What really matters is what is called the predictive value. How well does a test determine how an individual will perform? On top of that, we need to know how easy is it for some individuals to cheat this, or any other form of lie detection? Then there is the issue of the effect of changing the setting from a scanning room to real life. MRI based lie detection is not a scientifically robust process.

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The issues that have to be addressed are listed in the report of the meeting, which can be accessed via the SINAPSE website. One is *"There are many (often not well understood) implications involved when extrapolating from data derived from research studies obtained in groups of participants in focused traditional neuroscience research settings, to imaging results obtained from a single individual in a setting that may be very different to the original research environment."* We are all different, and our minds change from one setting to another.

When the first period of funding from the Scottish Funding Council was coming to an end, one of our big challenges was to make a bid to get support for continuation of SINAPSE from 2015 to 2020. All the pooling groups had been told that some limited funding might be available if matched by individual Universities, but no studentships would be supported. Perhaps this is another example of the redisorganisation syndrome. It wasn't good enough to acknowledge the success and keep going. This was Government money and so was in the firing line of reformists. At the time, the goalposts were moving away from academic excellence towards commercial exploitation of research with the short–term objective of boosting the failing economy. In Scotland, Innovation Centres were set up. As often happens with Government initiatives, this wasn't a gradual change. The funding going to pooling groups was reduced substantially and there was a radical shift towards new Innovation Centres. As I've made clear, I am not opposed to the development of scientific findings into devices or processes that will be of economic benefit. Far from it. Having worked in the NHS for so many years I fully appreciate that commercialisation is the best way to advance many of the research findings into routine everyday practice. The insulin pen, the heart valve, the powered standing frame, the Easycom; these were all commercialised. However, they weren't developed in the first instance with a view to commercialisation. They, along with many other devices, were developed to help patients and to solve clinical problems. Once they had been tried and tested, thoughts then turned to potential commercialisation.

Many of the projects that were boosted by SINAPSE studentships are likely to be commercialised at some stage. This is true of all the pooling groups. However, this process would follow its natural time course and so might take five years, or even ten to fifteen years in some cases. That's far too long for politicians of any party and so Innovation Centres were set up with a view to accelerating the transfer from research to commercial exploitation. The drive to encourage commercial development was laudable. What I took issue with was the magnitude of the step-function change. Less than one nine hundredth of the total funding given out by SFC goes to the pooling groups in total, and with that backdrop, surely a smoother transition could have been implemented.

After some negotiation around the use of our funding we were given special dispensation to part-fund five 'seed-fund studentships' to help us to engage with other organisations. We were grateful for this, but the cut from forty-six to five students was a major blow to one of our greatest strengths. We were encouraged to seek studentships from other funding bodies in the UK and Europe, but we would do that anyway and it misses a key point. Not only had the studentships been a superb way of attracting the best young researchers and providing training that was envied far and wide, but SINAPSE studentships were the glue that brought researchers from different Universities together. We had a rule that each student should have at least two supervisors from different Universities. The students benefitted, but so too did the supervisors and the projects that they were working on. Sadly, the collective badgering from all the pooling groups failed to convince those advising the Funding Council of the value of studentships. We had all tried, but we failed. More of the same was never going to be acceptable. There was too much spin.

Despite the drop in studentships funded by SFC, SINAPSE continues to thrive and to act as the focal point for medical imaging research in Scotland. There are now over 600 individual members and new ground-breaking research is underway. I'll describe briefly our five seed fund studentships to highlight the breadth of work and the many research themes. All of these projects have attracted additional funding from other organisations, and so the value of the contribution from the public purse has been doubled.

Improving diagnostic accuracy in Dementia - a project led by the teams in Aberdeen (Professor Alison Murray, who is now Director of SINAPSE) and Edinburgh (Professor Joanna Wardlaw). The research partner organisation is IXICO, a London based company whose '*mission, as neuroscience experts in clinical data management and analysis, is to improve the brain health of people with neurological disease through the application of digital technologies'.*

> Brain imaging is recommended in UK and international guidelines in the assessment of all patients with suspected dementia, both to try to diagnose the likely underlying disease causing dementia and to exclude potentially surgically treatable abnormalities such as a large bleed or tumour, which occur in a small proportion of patients. However, scanning on its own doesn't tell the whole story because individuals cope differently, with some able to overcome the disease for some time before developing clinically obvious dementia. This project aims to give doctors a more complete picture by integrating scan data with performance data. This combination will be much more powerful than scan data or cognitive testing alone when assessing the effectiveness of new treatments that are beginning to appear.

Assessing blood supply within the brain after a Stroke – a project combining neurology expertise in Glasgow (Professor Keith Muir) with a company based in Edinburgh (Toshiba Medical Visualization Systems Europe).

> The method of measuring blood flow in the brain using CT angiography was described earlier. This is used in stroke where blood flow to part of the brain has been blocked and it is important to know how many other routes are open. There is a network of arteries in the brain called the Circle of Willis. It's a kind of ring-road system allowing blood to get from one side of the brain to the other. At present the blood flow is assessed by experts looking at the scans. The objective of the project is to automate this so that it is more objective and reproducible.

Adding value to eye tests: Eyesight and dementia – a project led by researchers in Edinburgh (Dr Tom MacGillivray) and Dundee (Prof Manuel Trucco) and one of Scotland's leading small companies, Optos plc.

This project aims to improve the ability of routine eye tests to spot conditions such as Age-related Macular Degeneration (AMD) and Alzheimer's Disease (AD). Doctors have always been able to tell quite a lot by looking into our eyes. By looking at blood vessels in images of the retina it might be possible to spot tell-tale signs of AMD or AD. For AMD this would help to prevent vision loss and blindness, while for AD it would contribute to better diagnosis or to monitoring people thought to be at risk of developing the disease later in life.

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Pre-surgical assessment with ultrasound scanning in Arterial disease– this project, led by Dundee (Prof Graeme Houston) and Edinburgh (Prof Peter Hoskins) and the Dundee based company Vascular Flow Technologies, shows that SINAPSE is about more than just brain imaging.

Arterial disease can be made worse by abnormal blood flow and arterial wall stresses and stiffness, and this varies significantly between patients. Recent advances in ultrasound scanning enable this to be assessed, but this is not yet done in regular clinical practice. The project aims to establish routine ways to identify which patents would be most suitable for particular surgical procedures and which medical devices would be most useful. This will avoid unnecessary operations and improve the outcome for patients with leg arterial disease.

Taking EEG out of the lab: EEG and sport – a project led by Stirling (Prof David Donaldson) and Aberdeen (Dr Kevin Allan) linking with the Scottish Institute for Sport.

Until now, measurements of brain function have been conducted in relatively artificial and abstract laboratory conditions. For EEG (the electroencephalogram, a measure of brain waves recorded by placing electrodes on the scalp) the traditional limitation was that data had to be recorded using fixed equipment and movement during the collection of data had to be kept to a minimum. However, the recent development of small, light-weight, battery-powered EEG amplifiers means that the traditional limits can be broken. The focus of this project is to use the new mobile EEG technology to study the mental aspects of sports performance. Several sports will be studied, including golf, archery, shooting and curling. Microsoft claims that their Cloud helps golfers by analysing high-speed images of a golf swing. However, the swing is determined by how the brain controls the body. It makes sense to study the brain.

I was asked at one of the Pint of Science events if there would ever be totally new types of imaging devices, based on different physical principles. In the near future I think this is unlikely, but what is happening is that very significant developments of existing equipment are taking place. SINAPSE researchers are involved in several of these. For example:

Fast Field Cycling [FFC] MRI is being developed in Aberdeen. You should be aware by now that imaging of all types needs a way of getting a contrast between the properties of one type of tissue and another. With FFC, additional contrast is obtained by varying the strength of the magnetic field, which in turn alters the rate of loss of nuclear spin signal.

High field MRI using a 7 Tesla magnet is being explored in Glasgow. A higher magnetic field gives a larger signal and so better resolution and clearer images. Some of the pioneering work at Institute of Neurological Sciences has been discussed earlier. The INS is now based in the Queen Elizabeth University Hospital in Glasgow and the combination of academic research and acute health care delivery makes this an ideal setting to explore the potential clinical benefits of high field MRI.

New fabrication techniques are enabling very small ultrasound devices to be produced. An example of this is the **Sonopill** project at the University of Glasgow. The Sonopill capsule travels through the gastro-intestinal tract, enabling very localised images to be produced.

As described in the sports project, **mobile EEG devices** that can be used outside the constraints of a science laboratory are now available, and pioneering work in the use of these is underway at the University of Stirling.

SINAPSE was not the organisation originating any of these exciting innovations. They are the work of individual groups within the partner organisations. The role of SINAPSE is to help the groups to further develop and exploit the innovations. They are far too valuable to be used by a single institution. Additional expertise can be accessed, and additional funding can be attracted by collective bids from two or more of the partner universities.

I was delighted to learn recently that SINAPSE has successfully produced its own brand of gin, ImaGin. ImaGin is a good source of iodine, and you'll know by now that iodine is used in CT scanning of blood vessels because it is good at stopping X-rays and in SPECT imaging because some of its isotopes give out gamma rays. ImaGin is well worth a try. £5 per bottle goes to medical research and it's available from *www.strathearndistillery.com/product/imagin/.*

Cheers!

Chapter 6: SPINNING THOUGHTS

It would be inappropriate for me to conclude by claiming that, having spent forty-seven years working in settings where medical imaging technologies have been used for healthcare, I am now a world expert and would be well placed to produce a list of guidelines. How healthcare technologies should be developed and managed now is not necessarily the same as how this was handled forty years ago, or even twenty or ten years ago. The times are a-changing. What I shall do is to meander round a few topics and reflect on aspect of these that influenced me through this random walk, for better or for worse. I've included this section to stimulate thought and discussion rather than to pontificate. There will be no list of recommendations. This is simply a reflection on some of the issues that I've encountered and some of the opinions that I've picked up. The extent to which the work settings have influenced the opinions will always be a matter of conjecture.

Choosing A Career

There are known knowns. These are things we know that we know.
There are known unknowns. That is to say, there are things that we know we don't know.
But there are also unknown unknowns. There are things we don't know we don't know.

Donald Rumsfeld

Out of all the options available to physics graduates at the time, why choose to work in healthcare? An answer that's often given is that it is good to work in public service and that improving health is a noble objective. Both are true, but perhaps citing these as the main reasons for choosing this profession is being slightly disingenuous. What drove me into medical physics, and kept me there for forty-seven years, is the fascination. As in most branches of science, those of us working in medical research find that there is far more that we don't know than we do know. We know more than we did forty-seven years ago, but much of this new knowledge has taken us to depths that we previously didn't know existed and this throws up many more challenges. The more you know, the more you know what you don't know, and this applies to most pathologies.

We know a lot more about Alzheimer's Disease than we used to. When I was a teenager the term often used was 'losing the place'. This was descriptive but not helpful. We now know about the amyloid plaques that build up between nerve cells in the brain and the tangles, which are twisted fibres of a protein called tau that form inside dying cells, but we don't know how to prevent the disease and even treatments to slow down progression are only slightly effective. Genetics and lifestyle factors may influence the likelihood of developing Alzheimer's, or at least the age at which we develop it, but we are far from having a clear picture of this. It's vastly complex.

Medical science still has a very long way to go. I certainly don't want to downplay the achievements that have been made. Many patients with conditions such as heart disease, stroke or cancer will fare far better today than ten or twenty years go. Massive strides are being made in medical treatment. Everyone working in healthcare has one key priority, and that is the wellbeing of patients. Whatever your role, whether you are operating on their hearts, scanning their brains, or helping to make them comfortable, you get a buzz when it goes well, and you feel down when it doesn't. These are the highs and the lows. But for me there was a permanent high, the fascination that is brought by the quest for new knowledge and new understanding of medical conditions.

As a young medical physicist my mind worked overtime as I ran home from a day's work. I tossed around the day's results and tried to figure out why the techniques that we were developing weren't working. As time went on and I became more experienced, the tossing around of ideas extended to include pathologies and not just technologies. Why do some patients in neurological intensive care units deteriorate and other recover well? What's happening in their brains? Is it a build-up of pressure? How could we measure that safely? Faced with these puzzles, how could you fail to read up all you could to get a better understanding? How could you think twice about whether to work over

the weekend to set up techniques when the hospital was quieter? This wasn't a job, it was a fascination.

Perhaps the downside is that in general medical physics isn't a very emotional line of work. There are highs and lows, but the highs don't match those experienced by actors, musicians or sports stars. We don't have nightly curtain calls or standing ovations. Our anterior cingulates don't get activated to the same extent. On the other hand, the lows are nowhere near those experienced by surgeons who have the occasional bad outcome, or bankers who lose millions of pounds. We do our best to ensure that the technologies that are used in healthcare work as well as possible and the research into medical disorders is robust. Medical Physicists do care about patient wellbeing, but we are not what can be described as a caring profession. We do, however, respect all who work in those professions. Medical Physicists are working to improve medical treatment, but the 'care' in healthcare is vital. Patients are not specimens to be used in research and this should always be kept in mind.

The Career Ladder.

Spinning up the career ladder is not really within our control. In most careers we get on with our work while keeping an eye open for opportunities to jump to another ladder or move up a rung on the ladder that we are on. I had seven different jobs, but because of the centralised model for employment of medical physicists, the various moves didn't involve a change of employer. Eventually I reached the heady heights of having to interface with management. Was it then still a fascination, or was it just a job? The honest answer is a bit of both. My work still involved the use of healthcare technologies and it still involved teaching and research, but there was also a requirement to have more involvement in the NHS bureaucratic processes. It would be simplistic to rate the clinical and research sides of my work as fascinating and the management side as tedious, although there was undoubtedly a bias in that direction. Perhaps fascination is not the appropriate word to describe this work. It's necessary - very necessary. But the words that come to mind to describe my feelings are *frustrating* and *challenging* rather than *fascinating*. That side of the work was a job.

People who made the Ladders

As our careers progress we perhaps don't appreciate the enormous influence of those who built the spider's web that surrounds us; the leaders with vision and drive who set up the organisations in which we work. In the field of medical physics in Scotland, two individuals rise to the surface. I hope my friends and colleagues will forgive me for singling them out, but I don't think there would be much disagreement with my choice.

John Lenihan.

Schoolteachers and university lecturers influence your direction of travel as you try to find your strengths and weaknesses, but maybe it's your first boss who makes the biggest impact. Your first boss is the person who leads the organisation that you've chosen to work in. Has that person developed an organisation that is thriving? Is there a good feel to the place? Are there exciting people working there? Is the boss a leader, a role model? I couldn't have been luckier

John Mark Anthony Lenihan had set up a medical physics unit at the Western Infirmary in Glasgow in 1948. By 1953 he had been promoted to Regional Physicist for the West of Scotland and he held this post through various reorganisations of the health service, until he retired in 1983. I remember John as a very warm individual, but someone who was very demanding; of others, but also of himself. He set high personal standards. He would arrive for work well before 8:00am and would frequently be the last to leave. As dedication was engraved in his DNA he appreciated the efforts of colleagues who tried to keep up.

During his 'reign' the Department grew from a few scientists and technologists to over three hundred, and yet I really don't think of John as an empire builder. He wasn't trying to take over another bank to make a bigger and more powerful organisation. He was quite simply following his strong belief that technology had a role in patient care and that it should be introduced into this setting by people who knew about it. It was John who taught me that a medical physicist is never on top of his job. As soon as you have worked on one technology and built up a good understanding of it, a new one appears, and you have to become an expert in that. I'm sure this is true in many professions, but in medical physics it is particularly true. Medical technologies don't stand still.

I hadn't been in the Department for long when I was called upon to assist at a conference that John had organised. One of his personal research fields was neutron activation analysis, a technique where neutrons are fired into a sample to determine which atoms are present in it. Clearly this is used on samples taken from the body and not in live bodies. John worked with colleagues from France who were also specialists in this field and he had organised a conference in Glasgow. I knew nothing about activation analysis, but I was invited to the conference dinner to assist John in his after-dinner speech. His PhD had been undertaken at the University of Glasgow and had been on the topic of the physics of the great highland bagpipe. He had undertaken this work with a fellow student, Seamus MacNeill. As I mentioned earlier Seamus went on to become a university lecturer, but he also set up the College of Piping in Glasgow and was often referred to as the world's most knowledgeable piping aficionado.

John's after-dinner speech was on the physics of the bagpipe, and my role was to demonstrate the different types of music that can be played. So, when I heard *"Our piper will now demonstrate the slow march*", I had to play one. This went well through the six-eight march, the strathspey, the reel and the hornpipe, all expertly described by John. However, he then went on to describe the piobroch, the classical music of the bagpipe. Unfortunately, I hadn't progressed to learning a piobroch at that time, but this performance had not been rehearsed. I played a semi-random selection of notes, sufficient to impress our guests from France. At the time, I didn't know about intellectual property. Could I have claimed the copyright?

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For many years John was science correspondent for the Glasgow Herald and every Saturday there was a feature article where he described everyday activities and devices from a scientific perspective. This was my first encounter with what is called lay presentation; communicating science to non-scientists or non-specialists. The articles were invariably interesting, but what really appealed were the illustrations drawn by a friend that John knew from the Glasgow School of Art. It was the illustration that drew your eye to the column in the first instance. You looked at the illustration, smiled, and then went on to read the words to find out what it was all about. John, thank you for the idea. I hope it works here.

Many of us who worked with John are adamant that he would not have survived in today's NHS with the current management strangulation. It certainly doesn't boost morale, and is the reason given by many senior doctors for early retirement. The comments about NHS management in Henry Marsh's books are enlightening [20,21]. Life was different when John Lenihan embarked on his career. When new technologies came along John would go to the Health Board Headquarters to plead for more staff to manage the introduction of the new devices to the clinical setting. He didn't always get his own way, but he knew the processes, and they were relatively straightforward. In today's setting of

committees and complex management structures I think he would have fled to a university to concentrate on his research. He didn't like being messed around. *"Nemo me impune lacessit."*

Although John had set up the Clinical Physics Department in a building in the Centre of Glasgow that would serve as its headquarters for many years, he firmly believed that the majority of staff should be based in hospitals within clinical teams. There were no patients at the Clinical Physics Headquarters, and no clinicians. Physicists have to be integrated into clinical teams and exposed to the problems at the coalface. John set up an organisation that fitted into that setting.

John Mallard

The other pioneer was Professor John Mallard. John is well known for his contributions to the development of both PET and MRI, but I owe personal thanks to him as he helped in my career development, and I'm sure in the career development of many other clinical physicists. He was head of Medical Physics in Aberdeen when John Lenihan ran the department in Glasgow. Each was head of the best Department in the world – in their own eyes. They had a good working relationship, although this was perhaps helped by the 150 miles that separated the two Units.

JM, second from left, explaining MRI to a chemist

John Mallard was chosen to be the external examiner for my PhD. This alone is evidence that there was no great hostility between the two best departments in the world. A few months before I was due to complete my thesis his group had published a paper in the Journal Physics in Medicine and Biology about conditions for high-resolution radioisotope scanning. They were claiming that in theory it should be possible to detect 1mm diameter volumes in the body that had abnormal concentration of a radiopharmaceutical, for example small blood vessels should be able to be detected. A group from the Hammersmith Hospital, and my supervisor Frank Gillespie and I, thought that this wasn't quite right, and had letters to that effect published in subsequent editions of the journal [26]. The problem was a very simple one. The Mallard group hadn't taken account of the amount of radioactivity that would be required. This would have to be far higher than the amount that could be injected into a body. We were right.

"Here lies the body of Sam McVey
Who died defending his right of way
He was right, dead right, but now he's gone
He's just as dead as if he'd been wrong."

Epitaph on Louisiana gravestone

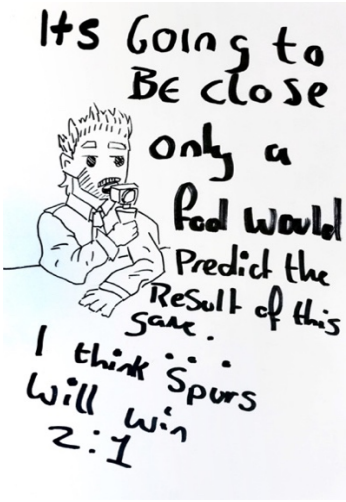
However, even if we were dead right, when I learned that Prof Mallard would be my external examiner, our letter didn't feel too clever. I shouldn't have worried. Good scientists don't hold grudges, and John Mallard was a very good scientist. The thesis was OK.

In 2013 I was honoured to be invited to deliver the eponymous John Mallard Lecture at the UK Radiology Congress in Liverpool. I've a feeling that Anna, who was a trainee student in Glasgow before moving to New York, Cambridge and then London, was behind this. It is an annual lecture sponsored by the Institute of Physics and Engineering in Medicine. I enjoyed the experience of delivering lecture and also the thought provoking processes of preparing the material. It gave me an excuse to visit John at his home in Aberdeen. Although well into his eighties, he was as bright as a

button and enjoyed reliving his experiences with PET and MRI at the University of Aberdeen. What really brought a sparkle to his eye, however, was recounting his battles with the University officials who had threatened to reorganise his department. Redisorganisation! John was having none of it. He threatened legal action and the University backed off – until he retired.

Prophesies

The title that I was given for my John Mallard talk was '*The role of functional imaging in the study of neurological and psychiatric disease: New developments and future prospects'.* I was being asked for prophesies. As we all know, predicting the future is a tricky business. I remember many years ago listening to advertisements on one of the pirate radio channels for the Horace Batchelor 'Infra-Draw Method'. This was a technique to help predict the results of football matches. I couldn't help thinking that if the method was any good then Horace wouldn't have to resort to advertising it on radio. He would just use it and cash in.



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Was I the best person to be making predictions? I was once asked by Angus McKay after one of our Health Technology Board for Scotland meetings why there wasn't a scanner that combines PET and MRI. Most new PET scanners at the time were being made into a single PET-CT scanner that offered the best of both worlds. PET gave information about physiological processes in the body and CT gave precise anatomical images to give a better indication of where the PET signals were coming from. So why not make PET-MRI, because MRI gives better tissue contrast than CT? I went on at great length to explain why this simply wouldn't happen because the magnetic field of the MRI scanner would interfere with the signal amplifiers in the PET scanners. This was about 12 months before Siemens brought out a prototype PET-MRI scanner with redesigned amplifiers. Scientists love a challenge, so never say never.

Here are three of my predictions from the John Mallard lecture:

1. New PET tracers will advance our understanding of many diseases and treatments. Tracers are appearing that can accurately detect beta amyloid, and tau proteins in Alzheimer's Disease, cell turnover rate, and low oxygen levels in tumours, and a wide range of transporters and receptors in the brain. I illustrated one of these earlier when describing how drug action can be measured, and two of our Neurosciences Foundation students are working in this field.

2. That brain imaging, in particular using the new techniques that detect connections in the brain, will become increasingly important in psychiatry. Around the time that I gave the lecture Thomas Insel was head of NIMH, the National Institute for Mental Health in the USA. Interestingly, Insel was soon to resign as the director of the NIMH to join the Life Science division of Google X. A new guideline called DSM5, the Diagnostic and Statistical Manual of Mental Disorders, had been released by the American Psychiatric Association. DSM5 met with considerable criticism [27], including suggestions that it was unscientific, lacking in objectivity and too heavily influenced by action groups and the pharmaceutical industry. In an attempt to add constructive debate Insel stated *"Mental disorders should be diagnosed more objectively by using a combination of genetics, brain scans and cognitive testing."*

   We have been striving for this for a long time, but with very limited success. Someone who is experiencing psychotic episodes is most likely to have a completely normal brain scan, and there are no biomedical tests that can explain what is going wrong. Maybe this could change.

   For many years I lectured to junior psychiatrists who were studying for the MRCP examination – Member of the Royal College of Psychiatry. When I started around 20 years ago my lectures were

really of academic interest. They would plug gaps in general medical knowledge but would be of little help on a day-to-day basis. The exception to this was the use of PET or SPECT in dementia, but most of the trainees would be going on to work in fields such as clinical depression or schizophrenia. Scanning had nothing to offer them other than its ability to detect subtle differences between control subjects and large groups of patients. It was being used in research but was of little value for individual diagnosis.

This hasn't changed yet, but the signs are promising. The MRI techniques that map brain connections are showing up abnormalities. These alone might not be specific enough to classify patients and help to suggest treatments, but when combined with other measurements such as gene screening profiles and psychometric testing the information will become tighter. Encouragingly, techniques have been developed that make it easier to combine the MRI data with other measures using what are called connectomes[28]. So, my prediction was that imaging alone won't be sufficient to aid diagnosis in schizophrenia, but if scans can be put into a format where they can readily be combined with other objective measurements then it might become possible to diagnose mental health conditions more reliably and to study treatments more accurately.

3. That the GOLD technique and the ABL101 compound being marketed by Aurum Biosciences would improve acute stroke diagnosis and treatment. I described this earlier. The clinical trial funded by the Wellcome Trust has still two years to run. It might prove to be effective, and it might not, but it's well worth trying. It's good medical science.

So, three predictions; a commentary on developing medical technologies. Does this make me a pundit? I guess I chose the wrong career.

Real Doctors.

Much of my work has been with medical doctors and I've been asked several times if I regret not having chosen medicine as a profession. I remember one occasion distinctly. The remark was not directed at me, but at my mentor John Lenihan. I was at a Burn's Supper. As an exponent of the great highland bagpipe, I attended several such events most years. After piping in the haggis, I could relax with the rest of the guests. On one occasion I ended up sitting at the same table as an eminent Glasgow radiologist. He didn't work at the same hospital as me, but I knew him by reputation. To make conversation I mentioned that I was a medical physicist and knew several of his colleagues. He glowered at me and said, *"I didn't like Lenihan. I used to tell him he should have been a real doctor.*

He meant, of course, a doctor of medicine, rather than a doctor of science. I was tempted to respond by pointing out that if it hadn't been for scientists like, James Clerk Maxwell, Wilhelm Roentgen, Godfrey Hounsfield or John Mallard, or the many medical scientists who helped to introduce imaging technologies into medical practice, then he wouldn't have a job. However, it was a social evening, so I just said that I did like Lenihan, and changed the subject. However, do I regret not studying medicine? In general, medical doctors are paid more than scientists, but scientists are well enough paid, so that's not a factor. Scientists, however, will always be support staff, and medical doctors are at the forefront of patient treatment. Would I have liked that? Well, yes, but the honest answer is that I'm happy to have been a scientist. You should do what comes naturally, and for me that was physics.

Those in support roles perhaps don't experience the buzz when a patient in your direct care is restored to good health, but then they don't have to face next of kin when procedures don't work out. Special skill is needed for that, and I know that some doctors are better at it than others. I've worked with doctors who left me wondering why on earth they pursued a career in medicine, and perhaps they shouldn't have. Personality is just as important as intellect.

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Spinning wheels

Yesterday's the past, tomorrow's the future, but today is a gift. That's why it's called the present.

Bil Keane

You only live once. We all want to make best use of our time and often work can involve activities that are not the best use of time. Attending management meetings is not the only bad use of time. Commuting can be another necessary evil. For all of my working years I was fortunate in that I never lived more than eight miles from my place of work. I know of people who work in London and have a home just outside Dublin, or work in Edinburgh and have a home in the south of England. Needs must, and if that's what you have to do it can be done, but it's an added hassle.

For my various commutes I had the option of taking public transport, or going by car, bicycle or on foot. Driving was always my least favourite choice. Going for a spin in a car has little appeal to me. I'm a scientist and I'm supposed to be fascinated by technologies and how they work, but the very mention of F1 makes my blood boil. So, what's my problem with cars? Why have I never been interested in them? Today, the answer is pollution. Individually our impact is minimal, but we have to take responsibility for our actions and live the lifestyle that we believe to be best. That means don't drive unless you have to. However, the answer hasn't always been pollution. When I was in my twenties and thirties there was little focus on the environment, yet my commuting choices were still by going on foot or by bicycle. It just felt better.

My various homes over the years were all around eight miles by road from my place of work and it took just over half an hour to run to work. Sounds impressive, but my running partner and I could take several short cuts through parks and over golf courses, so it didn't take much longer than driving, and we didn't have to find somewhere to park. The only small snag with this routine was that eventually I would run out of fresh clothes. One day a week was change-over day. Going by public transport took ages, so I drove. Shame on me.

As the years went on my one hundred mile a week lifestyle became more challenging. Gradually I replaced running with cycling. Running is not for everyone. If you don't enjoy it don't do it. There are other ways of exercising. Cycling, on the other hand, is something that could be managed by many who have to commute less than ten miles. Why do more people not cycle to work? Sadly, the simple answer is that cycling is far too dangerous.

A moment that will live with me forever is when I learned that Hugh Wilson, one of my closest friends, had been killed while cycling to work. A lady who was taking her child to school by car had parked at the school gates on a main road and then opened the door, pushing Hugh off his bicycle right in front of a bus. Hugh had two young daughters and taught computing at a local college. He was one of my running mates. We met most Sunday mornings at 8:00 am before others were awake and ran for two hours. We ran at a comfortable pace, not racing but not hanging around either. The rule was that if you couldn't hold a conversation then you were running too fast. We solved all the world's problems. Hugh was loved by everyone who knew him and the world has been a much poorer place because of one act of thoughtlessness and selfishness.

I was car-doored, as it's called, a few years ago, but was more fortunate. I was taken by ambulance to hospital and couldn't walk properly for several months, but I wasn't hit by another vehicle. I was lucky. *"I didn't see you",* was the driver's feeble excuse, although I do have to say that he was very contrite and didn't hide. Now I always apply the four-foot rule. Assume that the door will open as you pass a car and allow enough space for it. I have been grateful for this many times.

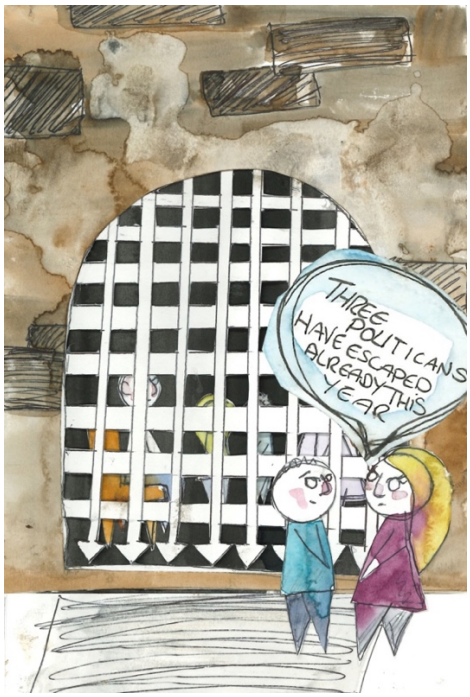
It amazes me that driving instructors and the driving test do not put more emphasis on exiting the vehicle. I believe that in Holland, for instance, trainee drivers are taught how to open the door. It's so basic. In this country you can pick up tips about how to get out of the car without showing your underwear, or how to ease the load on your leg muscles, but where are the adverts for safe door opening? The rule is simple. USE THE HAND FURTHEST FROM THE DOOR TO OPEN THE HANDLE. That ensures that you turn your body to a position where you are looking directly out of the door. Even if you didn't understand the explanations of CT, or MRI, or PET, please follow this simple take home message.

Why is this not part of the driving test?

Sadly, the tragic death of Hugh Wilson was only one example of this problem. There are countless accidents. Few regular cyclists can say that they have avoided them completely. Some accidents are the fault of the cyclist, but if you cycle responsibly and obobey the rules then you should be safe if you manage to avoid dangerous drivers, but sadly that is a lottery. It shouldn't be, but it is.

One of my colleagues at work spends much of his 'spare' time helping to organise an annual event called Peddle on Parliament - POP. The parliament in question is our devolved one at Holyrood in Edinburgh. Apparently, when the parliament was first set up, the capital of Scotland didn't have a suitable building, so they had to construct a new one. We had a castle waiting there.

POP involves thousands of us cycling down the High Street in Edinburgh. We then congregate at the Holyrood building where there are plenty of posts to chain your bike to, and there we listen to speeches. Usually this starts with one or two short talks given by cyclists. My favorite was delivered by Graeme Obree, the *Flying Scotsman* who twice broke the world one-hour cycling record on a bicycle that he built himself and included parts from an old washing machine. Impressive technology development! Graeme made an impassioned plea for extra funding to make cycling safer and pointed out that this shouldn't be looked on as expenditure, but as investment. Scotland should be a haven for those who like cycling holidays. We have the scenery and a good mixture of flat land and hills, but we need good road surfaces and safe cycle routes. Also, if we can increase the number of cycling commuters then we would ease the strain on public transport and reduce pollution. Well-said Graeme. Then the politicians speak, and I'm afraid I switch off. I get manifestoed out.



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The event raises awareness of the issues and this can only be good in the long run, or the long cycle. Cycling in cities is now much safer than it was twenty years ago, but it's still more dangerous than it should be.

Another problem is that we have appalling road surfaces, and this affects bicycles more than cars and lorries. Last summer I cycled in France and the difference was stunning. The roads were smooth and the attitude of drivers towards cyclists was totally different. We discussed this and concluded that it wasn't just due to freezing weather affecting the road surfaces but was down to cultural differences.

It is simply that cycling is respected more in France than it is in the UK. It shouldn't cost money to change that. What are Facebook and Twitter for?

Changes in Working Practices

Spin is the theme of this book. Whether it's nuclear spin, organisational spin or information spin, we live in a revolving, and an evolving world. However, by far the greatest change in my working practice, and in the working practices of most of us, is the result of advances in computer science and information technology. My PhD thesis had to be typed, and then re-typed. I had to get it right the second time because I couldn't afford to pay for a third typing. In our everyday work, we wrote letters that were submitted to the typing pool. When they reached the top of the pile they would be typed and come back to us to proof-read. Mistakes, usually made by us and not the typists, would be corrected. The process would be repeated, an envelope would be typed and the letter posted. Sometimes, when a reply came back, it was a struggle to remember what the letter had been about in the first place.

If we wanted a reprint of a scientific paper we had to go to the University library, which was several miles away, fill out a form to be sent to the National Lending Library, and then wait for many weeks for a photocopy of the paper to arrive by post. Academics can now get access to most of the scientific literature within minutes and have a copy of a published paper on their computer screens in a format that can be searched for key words. We do our own typing and Microsoft corrects our mistakes - or introduces mistakes. You do have to be careful with predictive text.

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Processes that took weeks now take minutes. A doctor can access a patient's full medical history on-line. Added to this, the doctor no longer has to remember all facts about a condition. Quick reminders are available through trusted internet sources. You have to be careful which sources of information to use, but they are available.

There can, of course, be a downside to internet communication. At times it can be too rapid. It can reflect instantaneous reaction rather than a considered appraisal of an issue. You read: "*This morning the US President tweeted ……..*" We don't want to know his instantaneous reaction. We want a considered opinion after consulting with leading authorities on an issue. Perhaps Twitter postings should have a delay loop of a few hours before they become public to allow time for considered reflection.

I've already discussed the advances in person-to-person interaction. No longer do we all have to be in the same room. We can have teleconferences with colleagues, across the city, or country or globe. Certainly, the occasional face-to-face meeting for social bonding is helpful, but otherwise we can interact on-line. Scientists generally work now in one of two places. They are in the lab or in front of a computer screen. If your specialty is medical image analysis, then you spend all of your working day in front of a computer screen. I hope that image analysts don't watch TV or play computer games.

Peer Review, Ethics and Fantasies

I mentioned earlier that my PhD supervisor and I had a letter published in a Journal in which we pointed out an error in one of John Mallard's publications. This points to an important aspect of peer review. How come a paper that had a fundamental flaw was published in the first place? Surely the science experts who reviewed the paper should have picked up on the flaw before it was accepted for

publication? In an ideal world, yes, they should have. But we don't live in an ideal world. Many papers are complicated, and reviewers don't have time to check all the calculations. Especially now, when computer modeling is often a key component in the analysis of data, reviewers might not have access to the very specialised computer systems that have been used in the study. They can't check the results. There are limits to the effectiveness of peer review, so it is common for papers to be followed by a series of letters pointing out flaws. There will always be strange findings that get sorted out over time. The detection of neutrinos moving faster than the speed of light was a classic example. Measurements can be flawed, but as long as there is open publication and others are free to comment it gets sorted.

What is not all right is when results are not published. If a pharmaceutical company funds a study and the results show that their drug is effective, then they want this to be published. On the other hand, if it's not shown to be effective, or worse still shown to be ineffective or have side effects, then the company might not be too keen on publication. Clearly this leads to a huge publication bias. A great deal of attention has recently been drawn to this problem through organisations like AllTrials [alltrials.net], TED Talks on the subject, and many press articles. It's being sorted, but this has taken a great deal of effort and shouldn't have been necessary. Ethical issues have different interpretations in the worlds of science and commerce. This shouldn't be the case, but we don't live in an ideal world.

In medical science we focus a great deal on ethics. Most scientists mean well, but can they get too carried away with the excitement of their developments? A common problem with new knowledge or new technologies is that we can't un-invent them, but it might not always be ethical to allow them to be used. We, struggle with this. Widespread use of genetically engineered crops and artificially produced embryos are current examples of dilemmas in life science, but physicists can look back to the ethical challenges raised by nuclear fission. With adequate waste disposal nuclear fission could be one of the cleanest ways of producing vast amounts of power, but in the hands of political extremists it could be a technique for mass destruction on an unprecedented scale. We can't un-invent it. Its use has to be regulated, and perhaps we're not great at doing that. We have to rely on having responsible hands on the nuclear buttons. *'We are a tantrum away from mass destruction'* is a phrase that I heard recently. And we have narcissists in high places. Oh dear! We have good processes in place for the small issues, like research study design, but what about the big issues?

Let's fantasize. Imagine a worldwide ethics committee sitting in Johannesburg in 1886. The members had arrived at their meeting on horse-drawn vehicles. One item on their agenda was to consider a new innovation by a Mr. Benz, a German engineer who had produced a petrol-powered automobile. There was strong opposition from the Union of Coachmen, but they were just trying to protect their jobs and so ethics approval was granted. It took only ten years before the first fatal road accident was recorded in the UK – Bridget Driscoll was walking with her teenage daughter and a friend in the grounds of the Crystal Palace in London when she was struck by a car. Ironically, the coroner's comment after delivering a verdict of accidental death was that he hoped *'such a thing would never happen again'*! By now well over half a million people have been killed on roads in the UK. Another problem that an ethics committee couldn't foresee in 1886 was that a century later the device would be responsible for one fifth of the emissions leading to global warming. There were no constraints, no regulations, and no pilot studies to look at environmental effects. Money took over and has ruled in this industry for the past 130 years.

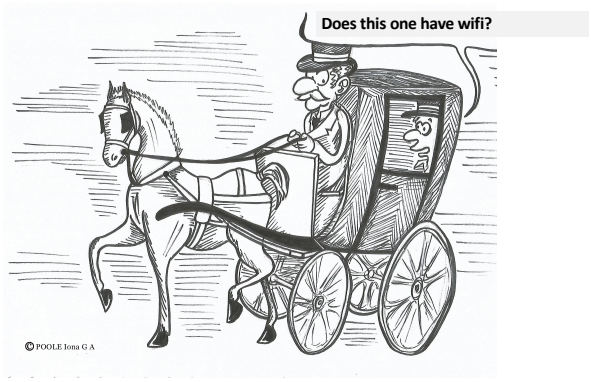
Remember we are considering an imaginary world here. John Lennon imagined a world free of heaven, countries, and possessions, but he didn't consider a world free of automobiles. What a stupid suggestion. How would we get around? Well, they were getting around quite well in 1886. It was slow, but they got there. When we looked at health economics we saw that quality of life measurements can be made. What would our quality of life be like without the automobile? Life would be very different, but would we be less happy or feel that life is less fulfilling? This is of course complete fantasy, but it does illustrate the dilemmas that we face, but don't always face up to.

Technology has led to many of these dilemmas. Can it help to mitigate some of the consequences? Take climate change as an example. We are making progress. Measures are being put in place to limit the use of fossil fuels and even if one irresponsible national leader is ignoring the guidelines, most countries are doing their bit. Technologists thrive on challenges, and so far in our history they have

shown that what was previously thought to be impossible can become routine. We can combine PET and MRI into a single scanner; we can put powerful computers in our pockets; people have walked on the moon. Set technologists a challenge and they are likely to meet it. So, if that challenge is to clean up our planet, then we should have confidence that the technologies that will be needed will be developed.

Perhaps, however, a bigger and more uncertain challenge rests with social scientists and politicians. Can public awareness of the issues be raised? Can the public be persuaded that looking after our planet is more important than driving your child a few hundred yards to school? Will there ever be acceptance that we are chronically overpopulating our planet? Will the public and politicians ever be persuaded that the state of the earth 100 years from now is more important than what is done in the next few years, or the next term in office? On this issue I'm afraid we have to be less optimistic. Politicians are tuned to think short term, and we shouldn't blame them. They work within the processes that we have established. These are not the laws of physics, they are the laws of society. When you look at the enormity of the challenge facing social scientists, then perhaps those who specialise in physics are taking the easy option.

Only time will tell if my paranoia about the future of the planet is justified. What is clear, however, is that in so many areas, we are completely out of control. Consistently, however, I've been arguing against control. We should have freedom to develop MRI and CT scanners, and we shouldn't have managers breathing down our necks constraining our every action. We should be trusted. Perhaps that's what it comes down to. Trust us, and we shall self-regulate. To do that effectively we need information. The imaginary world mentioned above, where there are no petrol driven vehicles, would be a paradox. Physical movement from place to place would be extremely slow, but the movement of information would be virtually instantaneous.



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It is now mainly electronic networks that are our sources of information, and so self-regulation can now be quite well informed. A great deal of information sifting is needed, and we have to consider the validity of our information sources, but there is hope. With this information we should be able to self-regulate better than previous generations. We can all constrain the products that we buy. If they come from a company or a country that we have issues with, then we alter our purchasing habits. We can change our activities if there is convincing evidence to persuade us. This is happening. More parents are walking with their children to school, more workers are cycling to work, more employers are encouraging flexible working hours, more shops are stocking locally produced produce, unethical commercial practices are being exposed and purchasing patterns are altering as a result – not enough, but it's a start. A world without cars is a fantasy, but perhaps a world where we are well informed and can use our own judgement isn't a fantasy.

This is one reason why the communication of science to the public in general is so critically important. We are all in this together. Our planet is the responsibility of us all. We all have a role in decision-making, but to do this effectively we have to be well informed. We need to develop skills in judging the authenticity of information. Maybe this should be taught more in schools and universities?

We Are All Different

We have had a look at the development and use of a wide range of medical devices, and a peek into the mind of someone who has worked with the technologies and with the people who use them.

Perhaps it would be appropriate to conclude by looking at the impact that these have made on people's lives. Robert L Weber's anthology '*A Random Walk in Science'* looks at many aspects of the interaction between science and society [29].

Section 73 is particularly interesting. There he describes, in detail, an experiment undertaken by James Prescott Joule at 6pm on Monday 31st May 1841. Joule describes connecting one terminal of a battery to the right cheek of a lady and the other terminal halfway between the chin and the ears. *This went on for around 13 minutes during which she felt a pricking sensation, a tremulous feeling all over the face and neck, and a strong taste in the mouth. The terminals were removed when she felt a very strong action through the head, her eyes shut, she quivered very strongly, and then she fainted. It was thought advisable to terminate the proceedings at that stage.* There is no record of why this was done. It could have been a scientific experiment on a volunteer, or, perhaps more likely, an early attempt at electroconvulsive therapy.

One hundred and seventy-six years later, similar experiments are still being done. In '*Override*' Caroline Williams describes her attempts to improve aspects of her mind [30]. She tackles executive control, spatial awareness, logical thinking and general anxiety. Some of her attempts to improve these functions involve the use of devices – a device that generates transcranial random noise to reduce her fear of mathematics; one that senses the direction of north and converts this into vibrations on a belt worn around the waist to improve her sense of direction; or one that involves wearing a headset that tracks the brain's electrical activity and so might help her to improve her mind control. Caroline is raising awareness of these rather than advocating that they should be used, and she has had fun exploring their potential applications. As this is about the mind, and we know so little about the mind, it's very much an open book. Perhaps not surprisingly the conclusion is often along the lines of '*this isn't for me'*, or '*I might try this a bit more'*.

The mind is very personal, but so is the rest of the body. Both the effects and the side effects of medicines vary considerably from person to person. Many medical scanners involve procedures that combine the use of the device with the administration of substances that can affect the body in ways that alter the image. Contrast materials such as iodine-based substances for CT or gadolinium-based substances for MRI help to show up blood vessels. MRI is regarded as being completely safe. It doesn't use radiation that could alter atoms in the body and as long as you don't have metal in your body you should be OK. However, what about the substances that are sometimes administered as part of the scanning process? Is gadolinium safe? Unfortunately, we are not too sure. Retention of Gadolinium could have adverse effects, especially in patients with poor kidney function. In July 2015 the FDA announced that it is investigating the risk of brain deposits of gadolinium from some of the materials that are used in MRI. The main concern relates to repeated use of these materials; four or more scans using gadolinium. I hope that investigations like this explore whether or not some patients are more susceptible than others. We are all different.

The basic scanning process in MRI might be completely safe, but that doesn't mean that it is a pleasant experience. Some of us welcomed it as a relaxing break from work when we volunteered as guinea pigs, but others find it very claustrophobic. It has been reported that one in six patients experiences claustrophobia in a scanner. The incidence is sufficiently high to have lead companies to develop scanners with larger apertures to lessen the likelihood of experiencing claustrophobia. So why are some patients more affected? Clearly this is down to differences in brain function. Ironically the nature of these differences could be explored using MRI if only we could get the subjects into the scanner!

The uniqueness of people, and indeed all organisms, perhaps makes biological science more challenging than physical science. We are all different, but one hydrogen atom is the same as all other hydrogen atoms. One positron is the same as all others. But wait a minute! Do we know this? Is it perhaps that physics hasn't yet reached this level of sophistication? Scientific 'facts' should always be challenged. To explore this further have a read at *Science for Heretics* by Barry Condon [31]. It's guaranteed to stretch your vision of science.

Medical technologies have undergone amazing developments over the forty-seven years covered in

these pages. Without doubt there will be many more developments over the next few decades. They will be the result of scientific endeavour, but their use should be regulated by a broad section of society. Those taking part will not need a detailed technical knowledge of the devices, but they will have to be in a position to understand what they do, what benefits they bring, and what risks are involved. There will have to be many debates, and they will have to take account of a wide range of issues. All that we can ask is that they are informed by peer reviewed factual data and not by spin.

And my final slide.

This is often the most welcomed phrase in a lecture. So here is my final slide:

I hope that you:

- *now have a slightly better idea how medical imaging devices work and what they are used for*
- *are more aware of some of the history of medical device development*
- *appreciate why research scientists and technologists are important in health care*
- *accept that bigger organisations aren't always better organisations*
- *have been able to count the number of times I've highlighted the hidden costs in complex bureaucratic processes*
- *see the benefit in having academic partnerships*
- *recognise the essential part played by small medical charities*
- *bought a new bike*
- *enjoyed fantasizing*
- *liked the illustrations.*

Please let me know.

And yes, I do have a secret about a senior civil servant, but don't we all?

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Acknowledgements

I've written scientific papers and reports but have never turned my hand to writing for a general audience. My friend and former colleague Barrie Condon is rather good at this. He has penned several sci-fi novels as Fergus Bannon and his non-fiction *Science for Heretics* is drawing wide acclaim. It's a 'must read' book. Barrie looked through an early draft of SPIN and suggested what should be removed (most of it) and what might be OK if it was tidied up. I needed this, so thanks Barrie.

The illustrations were a challenge. I thought it was a good idea to do something like this but lacked the talent to do it myself. Then another friend and former colleague David Sutton came to the rescue. David is the President of the Paisley Art Institute and so knows people. One of these is Alistair Strachan, an artist who teaches at the Glasgow Kelvin College. Al and his colleague Dominic Snyder decided that this would be an excellent first year project for the HND1 Art and Design students. To spice it up, prizes were offered for those judged to be outstanding. The results are stunning. Sincere thanks to all who contributed. Each artist is acknowledged alongside their illustration, but special mention should go to the competition winners. I've been taking part in Pipe Band Competitions for long enough to acknowledge that judging in any artform is subjective. The illustrations selected for prizes just seemed to fit best. The winners were: 1st Iona Pool;: 2nd Jillian Shearer; and 3rd Saffi Maguire. There were five other awards to; Jacqueline Forrest; Cara Heuston; Rebecca Johnstone; Nicole Gaffee; and Rachel Glen. And special mention for the contributions from Lauren McKelvie, Sarah Barr, Jack McGuire, Paris Brown, Agnieszka Siciarz. I hope that you all enjoyed taking part in this. It's for a worthy cause.

I've mentioned a few colleagues by name, but so many others came to mind when I was jotting down my thoughts. And the memories are fond ones. Thanks.