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Inaugural Lecture, 5th December 2005.

'Do you see what I see?'

Medical Imaging – the Interpretation of Visual Information

David Manning PhD MSc FInstP Professor of Medical Imaging

Abstract;

Röntgen's discovery of x-rays in 1895, gave to medicine the extraordinary benefit of being able to see inside the living body without surgery. Over time, technology has added to the sophistication of imaging processes in medicine and we now have a wide range of techniques at our disposal for the investigation and early detection of disease. But radiology deals with visual information; and like any information this requires interpretation. It is a practical field and medical images are used to make inferences about the state of peoples' health. These inferences are subject to the same variability and error as any decision-making process and so the criteria for the success of medical imaging are based not entirely on the images themselves but on the performance of the decision-makers. Research in the accuracy of medical imaging must draw on techniques from a wide range of disciplines including physics, psychology, computing, neuroscience and medicine in attempting to minimise diagnostic error.

Preamble

I feel immensely honoured and privileged to deliver this inaugural professorial lecture at St Martin's College, Lancaster for a number of reasons.

- ***professorial lectures are part of an important research tradition that this College is building;***
- ***I am very conscious of the work of those who have gone before me - on which my own work has built; and***
- ***it is an opportunity for me to thank those loved ones and colleagues, whose support over a lifetime, has led to this moment for me.***

My talk today is, to some extent, historical; in part, it's a journey through my research career to date. But I feel very strongly that the most exciting time is now. So

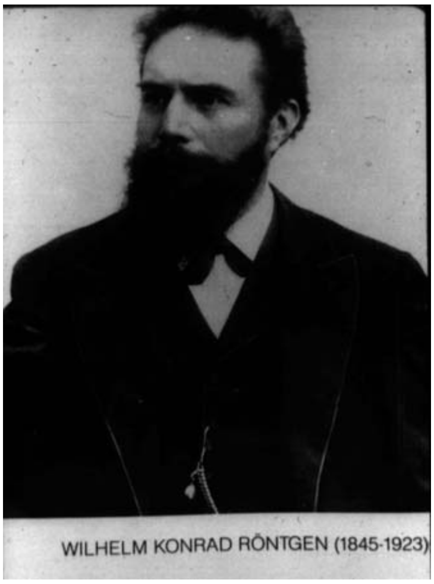
I hope to convey to you some of that excitement and I'll tell you some of the hopes and ambitions that I have for the future of research in the group of people I work with.

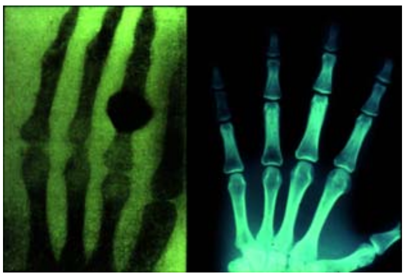
Introduction.

For a little over a 100 years medical imaging has made an important contribution to the diagnosis of disease and injury. It is a superb example of how science can be used for the greater good.

Röntgen's discovery in 1895 was a remarkable event. For experimentalists like him, the popular physics of the day was the newly discovered cathode rays.

One evening in November of that year the great man noticed that his cathode ray tube was producing an unexpected glow in a nearby fluorescent screen. He was intrigued by this but, being nobody's fool in matters of personal safety, he persuaded Frau Röntgen to insert her hand between the tube and the glowing screen. To his surprise and delight he saw the bones of his wife's hand projected in the fluorescence. Suddenly nature was allowing us to see with new eyes. For the first time in history one was able to see inside the living body without surgery.

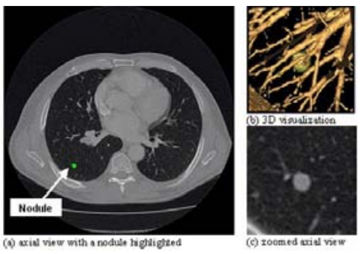




X-ray image of Röntgen's wife's hand and a modern equivalent

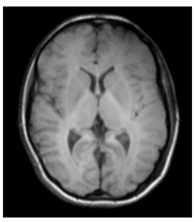
The medical applications of this new phenomenon were immediately apparent; so apparent in fact that within weeks the 'new kind of rays' were being used in clinics to diagnose bone fractures and by 1898 x-rays had found their military application - being used in medical field units at the battle of Omduman in the Sudanese war. The rate of development of medical x-ray techniques in the immediate years after their discovery was astonishing. And their implementation was rapid because their clinical utility was easy to recognise. As well as being able to see the skeleton and the air-filled lungs, contrast materials allowed visualisation of body cavities and blood vessels. Equipment quickly became more sophisticated, allowing real-time fluoroscopy of moving body systems.

In the century since those first advances many other technical improvements and innovations have emerged. Several of these have led to paradigm shifts in the way we carry out medical imaging. Radiopharmaceutical tracers were first used in the 1950s, image intensifiers transformed fluoroscopy in the 1960s, and ultrasound imaging had a similar impact on obstetrics in the same decade. Later on, computed tomography (CT) and magnetic resonance imaging (MRI) gave us unprecedented diagnostic capabilities through sectional imaging.



Enhanced sectional CT image and 3D rendering of the chest showing an early lung tumour

Positron Emission Tomography
(PET) Functional imaging with 3D reconstruction



Exquisite anatomical detail in MR brain image

But other techniques have had slower acceptance or have been controversial. This does not mean they proved to be useless but it is because their diagnostic advantage was too small to be immediately obvious; so some sort of testing had to confirm their value. In order to do this, criteria for improvement needed defining so that the level of improvement, if one existed, had to be measurably large enough for us to justify change.

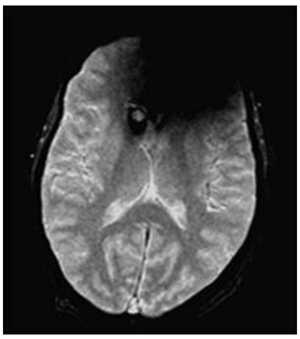
This brings us to an interesting point. To define criteria for improvement we need to be clear about what medical imaging is trying to achieve. Only then can we tell if it's underperforming.

The purpose of medical imaging is to provide visual information and reduce uncertainty.

Medical Image Limitations

Image information is visual, so we could define our criteria for improvement in terms of the quality of the information at the point of presentation to the observer. Medical images, like all visual data sets, have limits to what can be seen in them; so the information available will always be imperfect or incomplete. The limiting factors can be categorised:

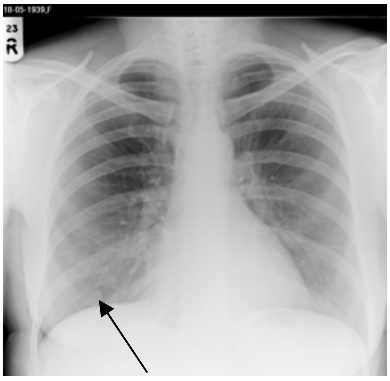
1. Artefacts. These are the pieces of visual information that are essentially man-made or created by the image-forming process. Simple examples include items of clothing but artefacts can also have complex origins in the physics of the acquisition process resulting in unsharpness and distortions.



MR image of the brain with the shadow artefact from a dental plate obscuring an underlying tumour.

2. Anatomy. Body structures overlap each other and obscure information that may be important to the clinical question. This is because the human body is a

three dimensional structure and we are creating from it a two dimensional image for display. This is a problem that has also given rise to technical developments such as CT scanning, Ultrasound, SPECT and PET. From the observer's point of view, too much information can be as problematic as too little however, and one of the ironies of medical imaging methods is that in presenting exquisite anatomical detail the pathology can become lost in a forest of 'structured noise'.



Conventional chest x-ray with an ambiguous overshadow (arrowed).
This was not a tumour but the right breast nipple.

3. Quantum limits. The information content of an image is proportional to its data density. But in practice there are a number of compromises that limit the ratio of the signal to noise. Examples of these trade-offs are the radiation dose delivered to the patient and the duration of the examination.

It is important to understand these limiting factors because they tell us something about the systems that produce the images. We can measure quantities related to them and derive figures of merit to compare imaging systems. For a physicist they are accessible and understandable; they are factors that can be modelled and quantified. But their relationship to diagnostic decisions from medical images is not well understood. Why that is so is because radiologists don't see physical quantities like contrast, resolution or signal to noise ratios; they see objects. And they interpret their meaning. So we should therefore add a fourth category to our limits list:

4. Observer limits

Human decision-making in measuring performance in diagnostic imaging forms a unique area of medical research. It lies at the intersection of a number of scientific disciplines but draws mainly on physics and psychology. The area has become known as the *psychophysics of medical image perception*.

Medical Image Perception

Radiology is highly practical. We use images to make inferences about the state of the health of patients and we judge the success of an imaging technique not solely on the images themselves but on the radiologists' performance and its effect on patient management. This is a perceptual process. So the success of medical imaging depends on factors that influence the ability of the observer to interpret the information. These factors fall into two broad classifications related to perception:

1. Those factors that are *image dependent* and relate to the visual conspicuity of relevant clinical features, and
2. Those that are image *independent*; are perceptual or cognitive and relate to what the observer knows about the visual information in front of him.

We have developed a wide range of monitoring procedures and tests that lead to good presentation of image features. But we know less about the cognitive factors that influence perception and allow the observer to structure the task of interpreting those features.

Improving Diagnostic Performance

How interpretative performance can be enhanced is worth considering. First, the quality of the information and its presentation could be improved.

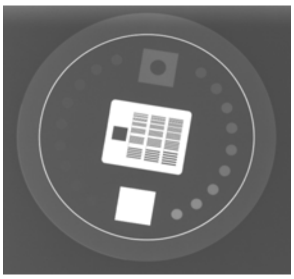


Image of one of the Leeds Contrast-Detail Test Objects.
Such tests can measure the physical properties of the image such as contrast and resolution.
But do they directly relate to diagnostic performance?

Radiological science has done well in this, using technical developments to the full, refining and diversifying information and presenting it so that features critical to the diagnostic question become visible.

Second, the taxonomy of those critical objects could be extended and more closely defined.

Radiologists have developed this part of the field extensively and continue to do so as new imaging methods offer themselves.

Third, the ability of radiologists to perceive relevant, critical features in the images could be improved.

Until the middle of the 20th century we had no concept of this possibility.

Observer variability

The work of Birkelo et al, 1947 was the first fully objective evaluation of medical imaging using observer performance data. Birkelo and his colleagues were trying to discern the diagnostic performance of traditional chest radiography compared with the (cheaper) mass miniature photo-fluorography. This was because there was urgent need of a population screening programme for pulmonary tuberculosis but it was proving to be very expensive. They were unable to show any performance differences between the two methods. And this was because inter-observer variance was so great that any variance between the imaging techniques was masked by the observer effect. They simply had no effective methodology to tease out the answer to their research question. An important consequence of the finding is, of course, that when disagreements take place between two people at least one of them must be wrong. An editorial accompanying their publication reflected the widespread surprise at this. It had never been considered until that point that expert radiologists might disagree with each other on fundamental decisions of diagnostic interpretation. What was even more surprising in subsequent studies by Garland (1949 and 1959) reflected on later by Yerushalmy (1969) was that the errors had unknown components and if the task was repeated, these errors were often recorded *within the same observer*. In other words, observers not only disagreed with each other, they disagreed with themselves. This situation has remained very much the same since that time despite all the technical advances we have seen; and we can conclude from this that the radiological task of interpreting visual information is a very difficult one. It is a noise limited decision making process and, what is more, the noise component is multifactorial.

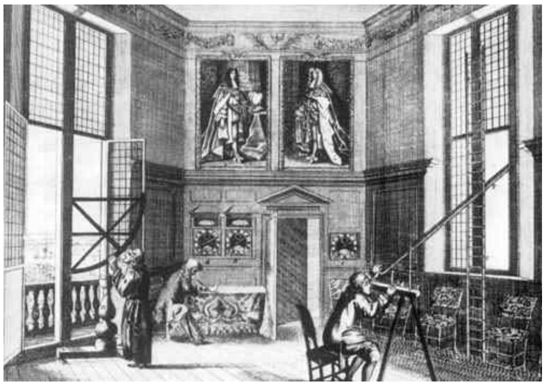
<u>Interobserver Variation</u>.

The earliest reference I could find relating to observer variation (error) in a scientific context relates to the Astronomer Royal, Nevil Maskelyne in 1796.

Maskelyne found that his observation of the transit of Venus was different to that of his assistant . The transit time was to be used to set ship navigational clocks with respect to the Greenwich meridian and their disagreement translated to one degree of navigation error. That error was an important constraint to navigational accuracy at sea. Maskelyne and his assistant tried to get their measurements to agree but after repeated attempts, they failed.

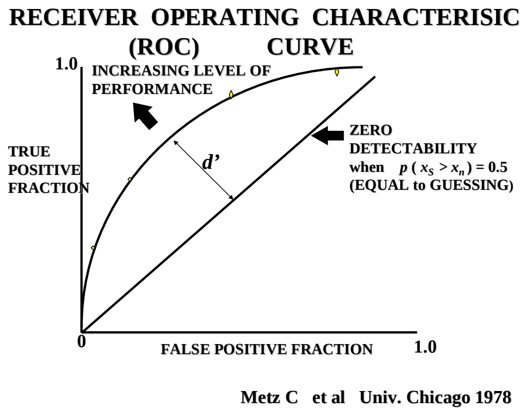
So Maskelyne sacked his assistant!

Nevil Maskelyne Astronomer Royal.



Royal Greenwich Observatory 1796

The study by Birkelo triggered interest in perception in medical imaging. A focus began to form on how and why differences in interpretation (ie errors) occur. This attracted the attention of various disciplines but the general trend was towards understanding visual decision-making as a statistically limited process. Psychology offered insight into modelling the components of interpretation, and physics gave methods for measuring performance through an adaptation of signal detection theory. Psychophysics was then in a position to offer the technique of receiver operating characteristics (ROC) as a realistic and rigorous method of performance assessment. Crucial to the theoretical foundation to all this was the work of Green and Swets in New York (1966), while Charles Metz and Lee Lusted in Chicago(1978) refined the notation and its applications to medical imaging. But the scientists whose work most influenced my thinking were those who took an experimental approach. They were the first to investigate the interplay between medical image features and their perception.



In this country, those people were John Mallard and Peter Sharpe from Aberdeen, Susan Chesters and Arnold Cowen from Leeds, and in America, Harold Kundel and Calvin Nodine, from Philadelphia.

Observer Experiments

In 1978 with Richard Carter from Lancaster University and Gordon Hamilton from Lancaster Royal Infirmary I was researching the problem of early detection of small liver tumours. Nuclear medicine was the best method at the time but the images took several minutes to acquire and the patients' respiratory movements often blurred the images. With the help of electronics engineers from the Engineering Department of Lancaster University we devised a motion correction device for the gamma camera at RLI. This appeared to improve the look of the images but we wanted to be sure that the device was genuinely improving tumour detection and not making it worse. So we set up a series of observer experiments using simulations of liver images and respiratory motion; it was our first attempt at signal detection and receiver operating characteristic methodologies.

The principles are these:

If we think of a particular disease state called 'positive' when the disease is present and 'negative' when there is no disease then the accuracy of a test can be represented in two descriptions:

i. Sensitivity or the True Positive Fraction (TPF).

This is given by the number of true positive decisions (TP) divided by the number of actually positive cases.

ii. Specificity or the True Negative Fraction (TNF).

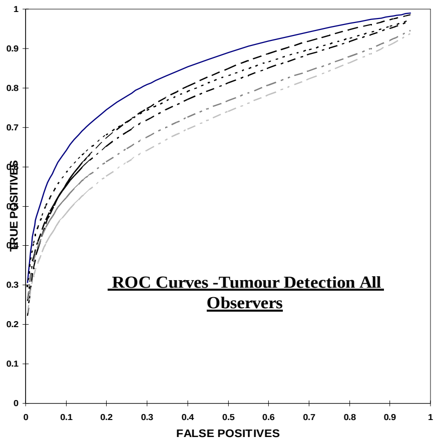
This is found by the number of true negative decisions (TN) divided by the number of actually negative cases.

There are only 2 other possible decision outcomes and they are:

False Positives ('yes, it's there' when in reality it isn't) and

False Negatives ('no, it's not there' when in fact it is).

With these principles taken from decision theory, and with the help of Professor Murray Aitkin from Lancaster University who did the statistics, we were able to determine performance under different conditions of weighting for motion correction using our device. It allowed us to select the optimum values for correction at different respiratory amplitudes and gave the potential for improving the early diagnosis of secondary liver tumours.



6 Motion Correction Weightings: Liver Tumour Images from γ-Camera

As with all things in medical science, events move on and CT and MR techniques soon replaced radionuclides as the method of choice for this diagnostic problem. But at the time we felt we had placed a small brick in the wall.

Later, working at King's College London with Philip Gishen using similar techniques to Birkelo's work, we were able to show that not all chest x-ray methods available at the time were equally effective in screening early lung cancer. This information gave practitioners an objective measure for comparing *diagnostic performance* of their techniques rather than simply measuring image characteristics.

By this time I was becoming more confident in the methods we were using. My move here to St Martin's College in 1995 coincided with some unique developments in the practice of radiography and radiology. For a number of reasons (mostly based on more effective use of professional skills within the health service) some radiographers were beginning to provide clinical interpretations of the images they produced. It was important for all concerned – especially the patients – that their performance was up to the standard of their medical colleagues. Precise measurement of their performance was essential.

For a scientist with an interest in measurements of diagnostic systems including the decision makers this presented some fascinating challenges.

First there were straightforward questions of the accuracy of alternative decision-makers compared with radiologists (with the help of Dr John Leach from Lancaster University we even tested the performance of an artificial intelligence system to detect simple fractures in x-rays). ROC methods seem ideally suited for this work.

Second, the radiographers needed specialised and intense training in their new interpretive roles. Questions surrounding the nature of training and methods of assessment needed to be addressed and our experience in analysing diagnostic performance seemed appropriate for this. In fact this work has led to important curriculum developments in both BSc and MSc degrees in radiography keeping our students involved in these research techniques as they engage with the findings.

But the deeper, less tractable questions were those on the nature of radiological expertise. How do radiologists do it? We know they do it imperfectly (they disagree with each other and with themselves on what they see) but at the same time they perform to an extraordinary level of accuracy and consistency day in, day out at a speed that defies belief. And they do this under time pressure and consequence of litigation if they get it wrong.

Do they see the world differently to the rest of us?

Could their brains have been 'rewired' by experience?

Or could it be that what radiologists do is not special at all and that we can all, instinctively carry out the skill if only we have the nerve?

Humans are inherently good at interpreting visual information. As a species we would not have survived this far without the skill. But particular perceptual skills are perhaps specific to the task and may not transfer well to other activities. We know for example that expertise depends heavily on specific experience that is recent and extensive.

So, as researchers we have become increasingly interested not only in differences in performance between observers (outcomes) but also on *how* they carry out the task (processes).

Eye-tracking experiments.

Recording the eye-movements of observers when they look at visual scenes can give insight into what is attracting attention. We can see what strategies they are using to search for hidden objects; and we can see what is being missed. These experiments are well known to psychologists and neuroscientists and in 1999 our research interest strayed into this territory. And we were able to pursue the theme through the PhD studies of one of our colleagues Dr Susan Barker-Mill.

Observer experiment using eye-tracking equipment.

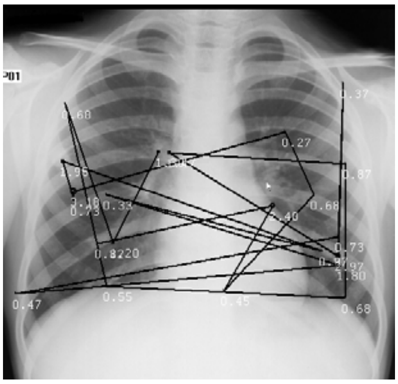
The fixation pattern acquired in a search for a fracture

The field of view in humans extends over 180° but it is only the centre of the field that provides sharp details. Consequently, we move our eyes (and heads) to bring interesting features into this centre. The pause over the point of interest is known as a *foveal fixation* and has a duration of about 200-300ms before we move our interest to a new location in a fast jump called a *saccade*. The eyes don't remain stationary for long before losing sensitivity; so where we dwell extensively on a location, fixations are characterised by spatial clustering.

Saccades are too fast for information to be gathered during their operation and so *eye-tracking experiments assume that fixations represent the location of conscious attention.* The path is the sequence in which image details are scrutinised; but fixation clusters illustrate the parts of the scene the observer finds most interesting. As a result, analysis of data from cluster location, dwell time and scan-path can give fascinating insights into how observers prioritise interesting locations. And it gives a good opportunity for comparing individual differences.

Such a research tool seemed an obvious way for us to probe some of the questions we were asking. But we needed expertise; and this is where the importance of the research community comes in. We knew of similar work being carried out in America and we had contact with these workers. We had also formed links with Alistair Gale – the UK's leading researcher in this field at the University of Loughborough. But we had success closer to home with the formation of what is becoming a highly productive collaboration with Dr Trevor Crawford at Lancaster University.

Together we have formed the Lancaster Medical Image and Neuroscience Research Group, LaMINeR. We are an unusual blend of scientists from psychology, physics, computer science, and medical imaging and with the invaluable collaboration of Drs Mike Flanagan, Alasdair Taylor and other radiology colleagues in the North-west we are probing some interesting questions.



The fixation pattern and eye movements from an expert radiologist searching for lung tumours.

RecentWork

For example; are disease features missed because they are not seen or are they missed because they are seen but misinterpreted? Recent work in this area has led us to believe that the majority of errors are made at the decision level and that relatively few pathologies escape a visual 'hit'. The implications of this are interesting. If observers make a visual interrogation of a feature we can be reasonably sure that the feature is displayed well enough for detection.

In a study to test out this theory we derived a mathematical description of the conspicuity of lung nodules in chest radiographs. Having a numerical index of visual appearance gave us the opportunity to see if intuition was correct – the more obvious the pathological nodule in the image the more likely it is to be called a lesion. In fact the results showed a poor correlation between visual conspicuity and observer confidence. It seems that although a more obvious nodule may be easier to *detect,* it is not necessarily easier to decide its pathological status. In other words better quality images may improve detection but not the decisions on the nature of what is detected.

We can assume then, that for the most part, medical imaging is achieving its technical goal of providing information. We know this because most missed pathology is seen in retrospect. But the resistant problem is a percentage failure of 'first-up' interpretation of the information. Solutions to this are unlikely to be entirely down to image improvements, although there are still important advances to be made in fundamental areas such as standardising the viewing conditions for radiology. There are probably important contributions to be made from education, computer aids, and a simple 'experience sharing' between readers in the improvement of diagnostic performance. All of these are concerned with the perceptual/cognitive component of the activity and are directed towards the decision-maker rather than the visual information.

Work in Progress

The research holding our attention at the moment takes both these approaches – observer based and information based – and is directed towards improving the accuracy of diagnostic outcomes.

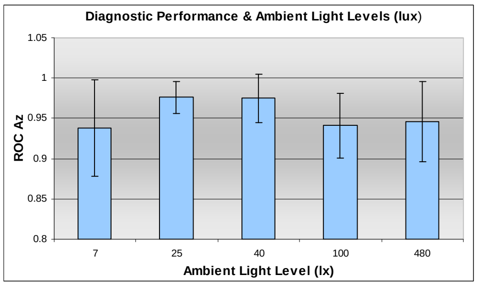
Feedback to observers

It is a discovery of eye-tracking studies that the fixation patterns used to scrutinise a visual scene are generally unknown to the observers. We have become interested in the idea that immediate feedback to an observer on the locations of his visual fixations might improve search strategies and diagnostic confidence. Early results from experiments indicate that in simple tasks requiring limited search, feedback improves the performance of inexperienced readers but reduces the confidence of those with more experience. It may have different effects in more demanding search tasks so the work continues in setting up observer eye-tracking experiments using complex radiological tasks. Our expectation from this work is a strategy for radiology and radiography training that allows learners a rapid feedback on the precision of their visual search patterns and the accuracy of their decisions.

Optimal viewing conditions

The use of cathode ray tube (CRT) monitors and liquid crystal display (LCD) panels for diagnosis in medical imaging is now common and will soon replace conventional film viewing. Digital imaging technology is developing rapidly and it is important with this technology that the image display is high quality. Work by colleagues in Dublin has shown that there is considerable variation in the quality of the displays, there are imprecise standards set for baseline performance, and that there is poor control of ambient lighting conditions in the viewing environment. These all represent perceptual problems for investigation. In a three-way collaboration between University College Dublin, Blackpool Victoria Hospital and ourselves we are investigating the effects on ROC performance of variables in the viewing conditions which eventually will contribute to the establishment of international standards for this important aspect of medical imaging.

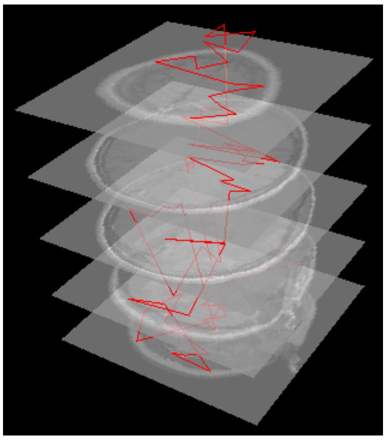
Environmental lighting conditions during a reporting session



Changes in diagnostic performance in different lighting conditions

Observer/display interaction

Associated with the problem of viewing environments for digital electronic images is the way that the observer interacts with the computer screen during a reporting session. Soft copy reporting is ergonomically quite different to the conditions of film viewing with a light box: there are more and different interactions between the reader and the device, the image sets are larger and more complex and there are image manipulation options available that can change the display for the observer. In addition to this is the potential for computer aided diagnosis (CADx) from artificial intelligence software allied to the image displays. Many of these activities are novel to radiologists and it is helpful, in the face of all the choices and activities available, to be able to determine the optimum settings and activities for a given task. To that end we are studying the activities of radiologists when they report on multiple sectional images in stack and tile presentations through their eye-movements and their decision performances. This is work that breaks new ground in observer experiments in medical imaging in that the eye-tracking techniques are applied to a three-dimensional problem as the observers scroll through large image datasets. The experimental problems will be unique and we expect to learn a great deal about our own experimental methods as well as the perceptual activities of the radiologists. But these are some of the key issues for image perception research for the next decade because for computer aided radiology diagnosis to be effective it is important that we have a clear understanding of how human visual perception and computer images synergise.



Eye-tracking observer activity with multiple sectional images stacked in display

Virtual colonoscopy with CADx prompt on a candidate polyp

<u>Future</u>

One of the most valuable assets we have gained as a group in recent years is the strength and diversity of our connection with the research community. The way this has developed is a tribute to the support given to our efforts from within our School, the Faculty and the College as a whole. As the Institution has grown it has become clear that there is a great deal to be gained from committing resource into research in niche areas of work. This enlightened approach has allowed us to develop our research reputation and commit ourselves to links with other workers. In some cases this has been an act of faith on behalf of those scientists from elsewhere who have joined with us on collaborative projects. But the rewards are now becoming clear; and I feel excited about opportunities that are offering themselves to us in a variety of projects in both applied research towards improving diagnostic medicine and in more fundamental questions in psychophysics and neuroscience.

Research encompasses a range of activities that increase the sum of what is known. It is work undertaken to increase the stock of human knowledge but is does not stop at that point. It is only valuable if it is shared and passed on. So we must always see research as part of a common enterprise which includes benefit to our students and the wider academic community. I feel confident that we shall maintain that ethic and look forward to a strengthening culture of research and scholarship within our College.

Acknowledgements.

To all the staff and students of Medical Imaging Sciences at SMC who have given their support and their time in many of the experiments we have carried out over the last ten years, thank you very much.

I am indebted to the members of LaMINeR, Dr Trevor Crawford, Tim Donovan, Steve Higham and Peter Phillips for their contribution to much of the recent work referred to here and to Dr Susan Barker-Mill whose PhD study gave momentum to our early research using eye-tracking. Dr John Leach was instrumental in guiding the final experiments of my own PhD in the 1990s which led to the current research direction. Phil Harris as Head of the School of Medical Imaging has been a constant supporter of my work and has been essential to the successful development of a research culture in Medical Imaging Sciences at St Martin's College while Drs Mike Flanagan and Alistair Taylor have given the priceless support of radiology to our efforts. Thank you all.

Dedicated to absent loved ones.

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Professor of Medical Imaging

5th December 2005