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Medical Imaging in the Digital Age: Fusing the Real and the Imagined

Keywords: human body, blood flow, medical imaging, 3D/4D, CFD, visualisation, simulation, virtual image

‘To predict the future we need logic, but we also need faith and imagination which can sometimes defy logic itself’, noted Arthur C. Clarke.¹ As we become more intimate with technology we realise how much our lives, and the understanding of our lives, has improved, while new questions and issues that need addressing were brought to light. Our particular work relies on the use of medical imaging and computer simulation technologies to enable the scientist and the physician to better the understanding of the human body and the ways it functions, by visualising phenomena otherwise not accessible to the naked eye.

Technology is an ubiquitous and versatile presence, well on its way to becoming a means of communication per se, while being the support of our culture as well as its fabric, the bond, the tie holding it together; a culture allowing the real and the virtual merging and blending harmoniously in our daily lives. In this paper we review aspects encountered in our own research, reflecting upon the changes in our perception of medical imaging, the developments (up until 2008) of the technology, and potential future paths to be followed or led by technology.

“[La méthode graphique] tend à élargir son domaine et à s’appliquer à toutes sortes d’objets, portant partout avec elle l’exactitude, la concision et la clarté.”

Étienne Jules Marey,
1865²

The search for the best way of understanding and then explaining motion and flow has preoccupied both artist and scientists for centuries. We are preoccupied with blood flow, one of the hidden-to-the-naked-eye phenomena, difficult to visualise, expose and explain. The need for a thorough examination lies in the tight connection between arteries, their vessel wall and the blood flowing through. Our research focuses on elucidating the role of fluid mechanic forces in cardiovascular disease and

treatment. Arteries adjust their calibre to maintain the level of wall shear stress, the frictional force exerted by flowing blood against the vessel wall. The endothelial cells that line the wall (cells that also respond to and express various molecular factors) mediate this behaviour. Atherosclerosis (fatty deposits in artery wall) and aneurysms (ballooning of artery wall) tend to develop at sites of complicated blood flow patterns. Their rupture, the event that precipitates most heart attacks and strokes, is determined in large part by the mechanical forces exerted on them. The success of vascular surgeries and interventions depends on the skill of the surgeon, the type of intervention, or the design of the medical device chosen, in order to avoid introducing further blood-flow-induced complications. With the discovery of the connection between flow patterns and circulatory system disease, computational fluid dynamics (CFD) experts have been brought into the team of experts that design and develop the techniques and devices used in various vascular interventions (such as bypass grafts, stents or coils).

The need for exploring unseen areas of the body has constantly been the driving force behind perfecting the medical visualisation techniques and technology. Arguably, it all began with Roentgen's accidental discovery of X-rays, which heralded the modern age of medical imaging. Soon thereafter, a well-designed experiment helped calibrate and adjust the apparatus and, within a month, angiography was born from the idea of replacing blood with a radio-opaque dye (Fig. 1).³

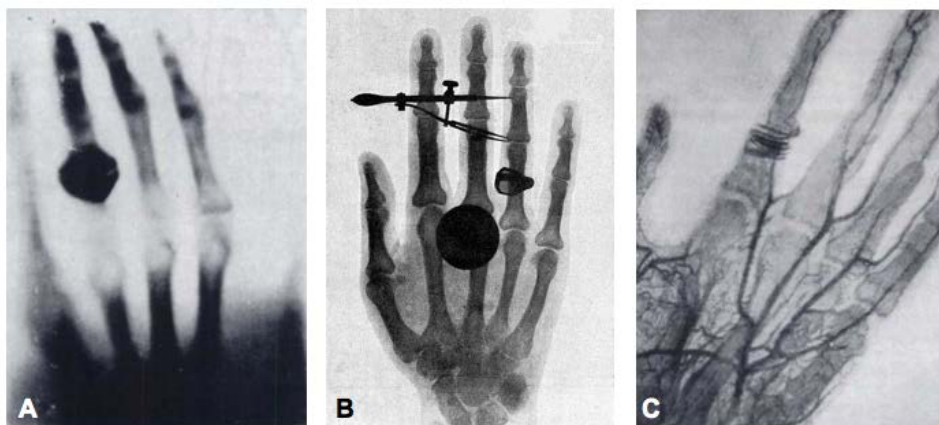


Fig. 1. Rapid evolution of X-ray imaging. After O. Glassner, 1934⁴

A: Roentgen's first x-ray. **B:** Soon thereafter, a marked improvement in image quality, and an attempt at calibration. **C:** Image of an amputated hand into which was injected a radio-opaque mixture — the first X-ray angiogram, less than a month after the first X-ray image.

The development of both technology and skills enabling visual depictions of blood opened new paths to a more thorough and detailed study of this very complex phenomenon of blood flow. Our own work, in the Biomedical

Simulation Lab at the University of Toronto, can be described as following multi-step process whereby from the reality of the human body and the physiological phenomenon of blood flow, a mathematical model is first created and then translated into a visual representation of the phenomenon observed; the last step is the refining of this image to make it understandable by the viewer, whether a trained expert or a layperson. To this translation process, which involves the evolution from a collection of binary data, to a sophisticated, clear, accurate visual rendering, the need to merge at both technological and communication levels is crucial. By unifying symbols and conventions, medical imaging technology allows for the creation of a valid 'meta-language', which allows not only an accurate representation, but also clear and fast transfer of information. This seems a natural path to follow since the ultimate goal is to use all the very complex blood flow data acquired locally in order to create a visual model as close to the 'body reality' as possible.

Those best suited to the task were the engineers, with their experience in visualisation of flow experimentally using physical models. As a result, the tendency for these models was to be symmetric and idealised for conceptual simplicity, but also practical reasons of manufacture. What engineers perceive as clear and easy to understand did not, however, fit the view of the clinicians, the main users of these models. To paraphrase Wendy Wheeler, progress of science and discovery, paralleled by the progress of language and vocabulary, can be achieved through lateral thinking and an open dialogue between engineers, scientist and artists.⁵

Thus, in order to make these models useful to clinicians, another visual vocabulary needed to be used. Over the centuries technology has proven itself supporting both artistic and scientific change, progress, and development. In all these guises, technology is malleable enough to adapt and strong enough to allow flexibility.

*"Why, sometimes I've believed as many as six impossible things
before breakfast." White Queen*

Lewis Carroll⁶

Blood flow representations have taken on very different appearances over the time. Considering the complexity of blood flow and the multi-faceted aspects of the surrounding tissues, interactions in the context of the physiology of the human body as a whole, and the challenges of representing it in a clear and accurate way, a transdisciplinary understanding of the issue was critical. To follow and understand the sequence of events, one has to know that the foundation for the mathematical model is Poiseuille's law⁷, according to which the velocity profile across an artery takes the mathematically simple shape of a parabola, making it easy to derive simple formula for wall shear stress. For nearly a century this law, which knowingly ignores the fact that blood

actually pulsates with each heart beat, shaped — and, as we will see later, still shapes — the perception of how blood flows. Womersley later extended Poiseuille's law to pulsating arteries, and his mathematical solution was readily accepted as a result of it being the fruit of the collaboration between mathematician (John Ronald Womersley, 1907-1958) and physiologist (Donald McDonald 1917-1974). The equations and their solutions are too complex to write here, but were shown to be the same as those describing electrical circuits. This led to a popularisation of electrical analogue models of the circulatory system, whereby resistors, capacitors and inductors could be tuned to model the complex relationships between flow (current) and pressure (voltage). As it is well known, the arterial diseases affect the nature of the pressure pulse. It was hoped that such models could be used to infer the nature of vascular diseases simply from pressure measurements.

By the late 1960s, a number of groups had suggested that the well-known localization of vascular diseases to arterial branches and bends could be only explained by the presence of complex blood flow patterns at these sites. This opened up a whole new line of investigation focused on local rather than global blood flow behaviours. Into this vacuum came engineers, with their experience in visualising flow experimentally using physical models.

Computer visualization has become an indispensable tool for mathematicians as well, and many mathematicians are currently collaborating with artists to invent ways to view previously unimaginable mathematical objects.

Robert Root-Bernstein, 1997⁸

Technology has always been a force supporting both the artistic and scientific progress and development. At the same time, what engineers perceive as clear and easy to understand may not fit the rest of the world's view. Thus, through collaboration between computer experts, bioengineers and clinicians, computer programs were created that made possible computer-generated images that not only reflected the data collected from the patient, but also represented it in a way familiar to the clinician. Current visual representations are considerably different from their recent predecessors, blood flow imaging having undergone, over the last decades, significant, distinct stages brought about by technological major advances.

First came the conventional X-ray angiogram based on projection of X-rays through body and onto a film. This particular approach did not allow easy visual access to arteries and blood (due to the presence of 'competing' radio-opaque bones). The introduction of computers allowed for digital vs. film imaging, and led to digital subtraction angiography,

where a 'mask' image acquired prior to contrast agent injection is subtracted, digitally, from images acquired during the injection of contrast agent.

The second phase, similarly, led to development of Computerized Axial Tomography (CAT) scans, allowing images of non-projectable slices (e.g., axial cuts through the body) to be reconstructed from multiple conventional projections. Nowadays 3D CT scanners provide sufficiently high resolution and image contrast to allow unambiguous detection of different tissues, including blood vessels, without the need for intra-arterial injections. This makes it possible to achieve photorealistic renderings of the digital data.⁹ While such medical imaging, along with magnetic resonance imaging (MRI) and ultrasound, are superb for anatomy, they remain relatively poor for function, namely, blood flow in our case. So, lastly, computer simulations of blood flow were used to fill the gap.

Beginning with the 1980s and the advent of desktop workstations, computational fluid dynamics (CFD), already an important tool in the design of cars and airplanes, was introduced to the study of blood flow. As the 1990s approached, medical imaging technologies, such as Doppler ultrasound and phase contrast MRI, began to open up non-invasive windows into "live" blood flow dynamics, albeit with relatively crude renderings. The situation in the mid-1990s was that CFD could provide intricate details of blood flow, but typically only for idealised cases, thus compensating for medical imaging's shortcomings in this area. This led to the development of so-called 'image-based CFD', whereby anatomical images could be transformed into patient-specific CFD models, thus providing a window into the 'true' blood flow patterns.

It is no longer a question of imitation, nor duplication, nor even parody. It is a question of substituting the signs of the real for the real.

Jean Baudrillard, 1981¹⁰

An interesting aspect of the computer-generated images is the simulation that allows the move from 'direct' (and sometimes limiting) use of patient data to the use of scientific simulation as a mode of investigation, through speculative extrapolation of data. We are thus placing ourselves in the post-modern age where the simulacrum precedes the original and the distinction between reality and representation break down. In our daily research context as well as in the clinic, for the most part, the object of our study became the simulated reality of the body. Medical imaging companies are seeking to deploy such seamless "image-based simulations", which will further blur the lines between the real and the virtual, allowing previously unimagined things to be achieved.

Technological developments are driving this increasingly seamless blurring of the lines between image and model. More broadly, these are examples of what Sarvazyan and colleagues call a new philosophy of medical imaging¹¹, wherein images acquired 'directly' from the patient are not used for diagnosis, but rather to refine computer-based models of the patient, from which the diagnoses are ultimately made.

Our daily research requires the translation of patient data into numerical data and then the generation of visual representations of blood flow that can serve two purposes: a) that of a model for a phenomenon or disease, or b) that of a model for an experiment (non-invasive way of determining the best treatment option). Hence, our work can be briefly summarised as in Fig. 2. The first paradigm involves the clinician's exposure to conventional visualisation drawn from a 'direct' medical image of the patient (with an intermediary 'virtual' step). The second paradigm adjusts reality through exposing the clinician to a virtual image, based on real-patient data, but drawn from a virtual patient, this time.

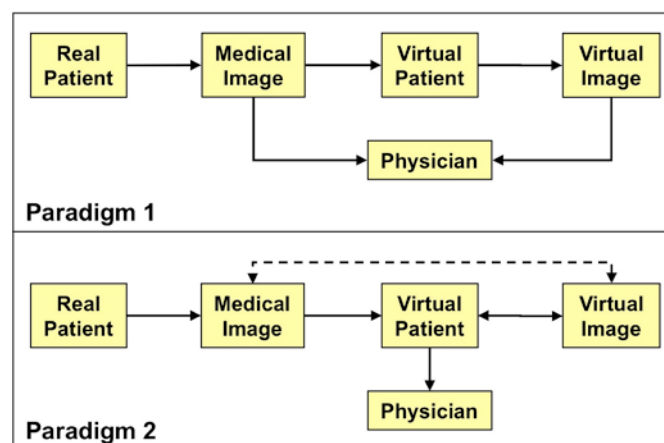


Fig. 2. Two paradigms in virtual imaging © David and Dolores Steinman

Paradigm 1: the physician is informed by the real and virtual images. Paradigm 2: the physician is informed directly by the virtual patient, now progressively refined until there is no difference between the real and virtual images.

We started, in the earlier years, working within the first paradigm using traditional engineering visualisations, but were soon using virtual imaging to portray results. (We define 'virtual imaging' as computer-generated images that are traditional medical representation look-alikes, as opposed to the particle path line movies we routinely show and which are virtual versions of traditional experimental engineering visualizations). Within this paradigm, virtual imaging is being used as an adjunct to conventional medical imaging. Computer simulations add 'knowledge' beyond what can

be directly or indirectly visualised. An easy analogy would be polling a few people, and using statistical techniques to infer the opinion of the population. If the right sample is polled, and the assumptions about the population are correct, the results of the poll are reasonable. Otherwise, however, the prediction could be totally wrong and, dangerously, it would not become apparent until too late, which in our particular case it would pose a critical problem to the clinician. Essentially, the clinician would use both real and virtual images to make a diagnosis or plan a treatment strategy, but would have to be aware of the possible traps.

Within the second paradigm, real images are used to construct a virtual patient and virtual images as before. However, in this case, we look at the difference between the real and virtual image and use that information to intelligently refine the virtual patient. Once the real and virtual images match, we can assume the virtual patient is a simulacrum of the real patient, and the clinician examining it may use it as a base for a diagnosis. As just one possible example, we would start with a normal brain virtual image, compared to a real brain image acquired in a patient. Assuming there is a bright spot in the real image, a tumour would be added to the virtual patient until the same bright spot would appear in the virtual image.¹² However, this is challenging because imaging is a 'lossy compression' of complex information, and the only way to restore that information is to add more information, say in the form of a model. As long as the model is correct the restoration is reasonable. However, if the model is wrong the reconstructed information is also wrong, in which case the clinician is faced with the same problems as in the first paradigm.

As a case study¹³ for the generalisation of individual information is the patient with a giant aneurysm, diagnosed by x-ray angiography, treated using a technique in which soft platinum coils are fed through the arteries in the leg, through the heart, and into the aneurismal artery. After six months, the coils had moved (or compacted), which is a common but potentially dangerous complication. Coils work by blocking flow into the aneurysm, allowing the blood to slowly clot and seal it from the inside. If the coils move or compact, the blood gets back into the aneurysm, allowing it to re-grow or potentially rupture. Our CFD simulation of flow, reconstructed from the high-resolution 3D X-ray imaging (using a particle visualisation technique inspired by engineering visualisations) showed that the high velocities during systole are in the same direction as the coils were pushed. (Circumstantial evidence for sure, but probably the cause). Perhaps given this type of information ahead of time, the clinician might have put in more coils or chosen either to put in more coils or a more invasive surgical alternative.

Because of the critical content of this information, used by the clinician in life-or-death decision-making, we had to convince ourselves that these simulations were valid and therefore developed virtual angiography¹⁴, in which a virtual dye is injected into the virtual artery, and then virtually imaged by virtual X-rays. Since there is no other way to validate our predicted velocity fields we felt that comparing real and virtual images would be the next best thing, what we call 'indirect validation'. Fortunately for everybody, the real angiogram compared well with the virtual one (see Fig. 3).¹⁵ To make this possible, we found we had to account for, in our virtual patient (i.e., CFD simulation), the fact that contrast agent is routinely injected at high pressure in order to completely displace the blood, albeit briefly, in order to maximise angiographic image quality. If we did not do this, the virtual and real angiograms did not agree as well. This modification of the CFD simulation to account for the injection, recognised only after comparing real and virtual images, reflects the steps in Paradigm 2. Conversely, the original CFD simulation, unperturbed by the contrast agent injection, may therefore be a better reflection of the real patient than the actual medical images themselves.

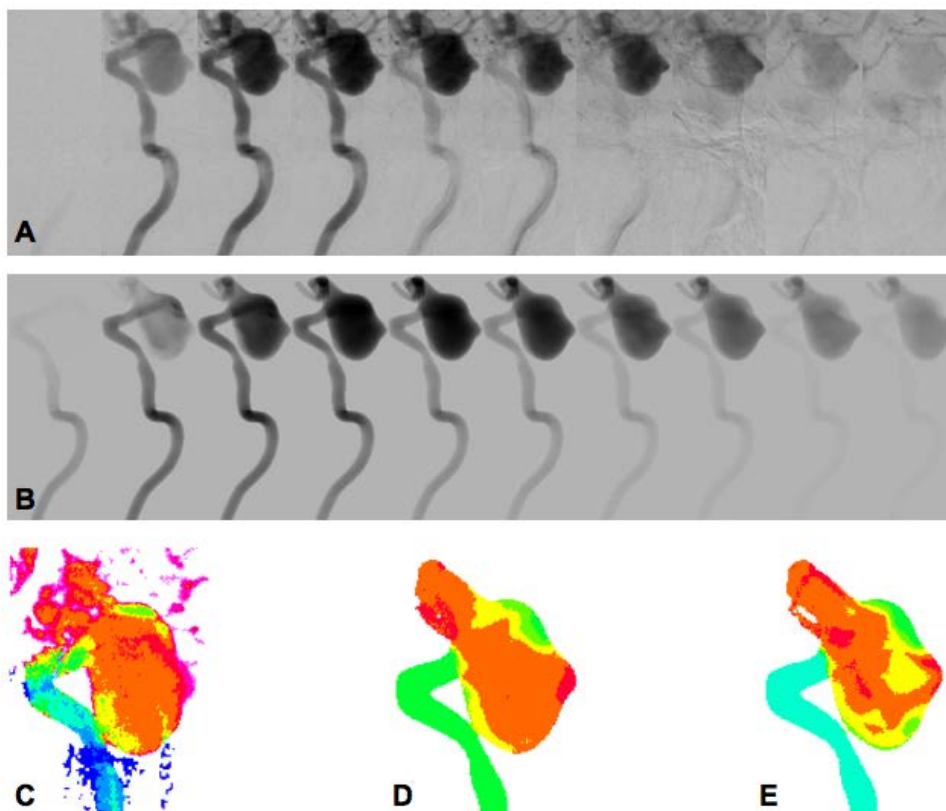


Fig. 3. Real vs. virtual X-ray angiography. © David and Dolores Steinman

A and **B** show the temporal evolution of X-ray contrast agent injected into a patient with a giant aneurysm (**A**) compared to a virtual angiographic sequence based on virtual contrast agent injected into a CFD model of the same aneurysm (**B**). **C** and **D** show the good agreement in colour-coded residence time maps derived from the real and virtual angiographic

sequences, respectively. **E** shows residence times based on a CFD model in which blood flow is undisturbed by the contrast agent injection. Representing the 'normal' state of the patient, one could argue that **E** is closer to the actual patient, despite it being virtual.

A further step is the translation back from the generalised model to patient-specific issues where simulation and reconstruction proved to be instrumental in explaining and exploring misunderstood phenomena and observations. The reality as represented by medical images is 'ever changing' or 'ever evolving'. Traditionally clinician and medical researcher alike were biased by the widespread clinical assumption of the 'fully-developed flow' that must behave according to Poiseuille's law if the artery is relatively long and straight. This assumption underlies many basic scientific and clinical imaging studies of vascular disease. Nevertheless, a number of incidental findings in our research caused us to question this. Most notably, as part of a collaborative study¹⁶ we were provided with magnetic resonance images of velocity profiles at transverse sections through the common carotid arteries of a large number of subjects. Although this artery, which brings blood from the aorta to the brain, is routinely assumed to be long and straight, the velocity profiles we observed were anything like those envisioned by Poiseuille (Fig. 4). Further investigation of these subjects revealed that in most cases their arteries possessed either very subtle curvatures around the area where the MRI images were collected, or, alternatively, stronger curvatures further away from where the MR images collecting site. Using CFD, we were able to show that such anatomic features were more than sufficient to give rise to the seemingly unusual velocity profiles observed.¹⁷

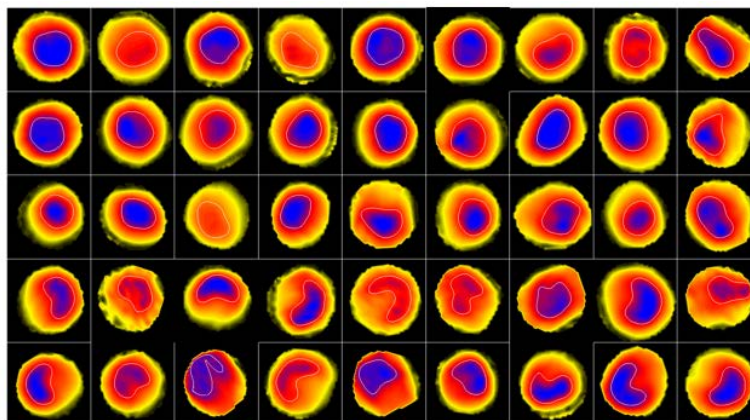


Fig. 4. Common carotid artery velocity profiles, imaged by MRI © David Steinman

The MRI data, normally presented in grayscale, were pseudocoloured to better highlight the shape of the velocity profiles. For Poiseuille flow, the shapes should be circularly symmetric, which is evident in only a few cases.

An important implication of this is that, if faced with such unexpected or unusual velocity profiles at a given point along an artery, it is all too alluring to assume that there is something ‘wrong’ with the patient, since their flow does not resemble the ‘normal’ flow described by the conceptually and mathematically simple model presented by Poiseuille. On the other hand, flow-related measurements in seemingly long and straight arteries may harbour large errors, being implicitly based on the assumption of Poiseuille flow within. Either way, it is important to establish a new mental model that supersedes that of Poiseuille in order to adjust to a new understanding of the actuality of the body as better uncovered through virtual examination.

Moving along the same path, and in continuous effort to replace the prejudice of what blood flow should look like, we have developed a simulacrum of the Doppler Ultrasound (DUS) examination (Fig. 5), which engages the user, both visually and aurally in a familiar environment, to help ‘train’ them to break their stereotypes. An additional use of the ‘virtual DUS’ is the streamlining of the DUS examination. Despite being a routine tool, DUS is very hard to interpret. Therefore, by developing an interactive, real-time DUS simulator we help in training sonographers, but also create a standardised platform to evaluate (accredit) their performance. Along the same lines of improving data collection and its interpretation (a representation closer to the actuality of the body) is the potential benefit of the DUS in the absence of any interference of tissue between the probe and the blood vessel. The image thus collected from the virtual patient becomes clearer and more accurate.

The machine does not isolate man from the great problems of nature but plunges him more deeply into them.

*Antoine de Saint-Exupery, 1939*¹⁸

The medical images we generate — with the aid of the computer — are truly reflections of a reality that escapes our view and our direct perception. As in the Buddhist myth of the origins of painting (in which Buddha’s first portrait was following his reflection in the water), paralleled by the Pliny version (the first portrait/visual representation being the outline of the Corinthian maiden’s lover shadow), the original visual representation is depicting (in) the absence of the object depicted.¹⁹

In many ways the role of the image over millennia has evolved without being fundamentally altered. Animal and human representations on cave walls seem to have had an informational purpose as well as a ritual one, while their mere presence was a constant reminder of the object

represented, but not present anymore. Later on, medical drawings, woodcuts, engravings played an explanatory role, but served also as a memorising tool. Information concerning living bodies through extrapolation of data collected through dissection was not only transmitted, but also fixed into the mind of the reader.

Since the Renaissance, students have been confronted with the reality of the body and its interpretations, through visual representations that were images of a 'normalised' body. Images became a certain reality, as perceived by the creator of the image: a corollary and a memorising kit. From Vesalius's *Fabrica*²⁰ onwards, anatomical representations become somehow more accurate through confrontation with direct experience. However, students continued to propagate the 'knowledge' from the printed image and accompanying text, which were not always accurately matching the dissected body. As we have shown in this paper, the current attitude towards medical images has not profoundly changed. These virtual imaging technologies we have discussed, where the virtual image appearance is good enough to make the doctor think they are real, are making inroads towards the stage where the model/virtual patient is manipulated iteratively until the real and virtual image contents are the same. At the same time, despite clear evidence and proof of the actual blood flow patterns existing within the various arteries depending on their particular geometry, the prejudice of what blood flow supposedly looks like in order to fit the Poiseuille model seems to continue to prevail in some clinical and scientific milieus.

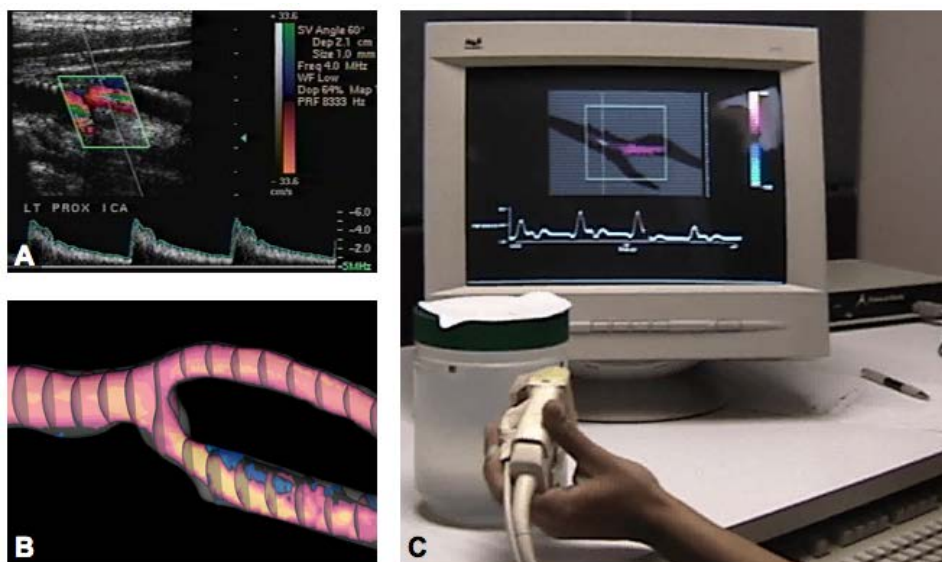


Fig. 5. Evolution of virtual Doppler ultrasound © David Steinman

A shows a screenshot from a real Doppler ultrasound examination. **B** shows a CFD model derived from the same patient shown in **A**. Here the CFD model is rendered using the CFD convention of planar slices, but is colour-coded using a pseudo-Doppler colour scale to highlight forward (yellow/red) and reverse (blue) flow. In **C**, a sonographer interactively 'examines' a virtual patient in the same way that they would examine a real patient. In this early prototype the

virtual patient is 'placed' in a peanut-butter jar; ultimately it will 'appear' inside a life-like mannequin.

According to Leonardo, the painted image has such an enormous power over the observer, that it can fool humans and animals alike.

Paul Z. Hartal, 1988²¹

Recognising the power and authority of the printed medical image, the trap we are trying to avoid is creating appealing representations that are misleading or void of meaning; our images aim at being as clear, accurate and precise as possible. Initially computer-generated images were normalised, average, generalised representations of the blood flow. The current trend is moving backwards: from the general to the individual. A paradoxically immense step forward in the medical investigation is the simulation that actually brings the clinician closer to the actuality of the patient than a direct investigation would allow. Making easily accessible the technology to physicians brings a lot of good, by enabling them to see the previously unseen. However, this approach carries a hidden danger: it implies several layers of intervention and requires a very careful and close control. Without appreciating the assumptions and inherent limitations of these technologies, a clinician is exposed to possible misinterpretation due to blind faith in the information received. 'No equations, however impressive and complex, can arrive at the truth if the initial assumptions are incorrect', said Arthur C. Clarke²², and virtual medical imaging is no different in that it can give the uninformed user (say the clinician interacting with the interface) the false sense of reality and truthfulness and potentially lead to great confusion or misunderstandings.

November 2008

Notes and References

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- ³ The example given in Fig. 1 is from a cadaver hand, but the principle of injecting a radio-opaque dye directly into the living artery, and imaging it via the projection of X-rays onto a flat plane, remains the gold standard for vascular imaging to this day.
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- ⁵ Personal communication, June 2008.
- ⁶ Carroll, L. (1911) *Alice's Adventures in Wonderland and Through the Looking-Glass and What Alice Found There*, Wool and Water, p. 205.
- ⁷ Jean-Louis-Marie Poiseuille (1799–1869) is a perfect example of transdisciplinarity, being a physician with a background in engineering. His pioneering experiments of

flow in capillary tubes laid the groundwork both for the quantitative study of blood flow and for modern fluid mechanics in general.

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- ¹² Of course it could be a different formation (a cyst), in which case other options would be tried and compared for consistency with other medical information (blood work, etc.). As Sarvazyan points out, the refinement of the virtual patient must be informed by other clinical information beyond the images themselves.
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