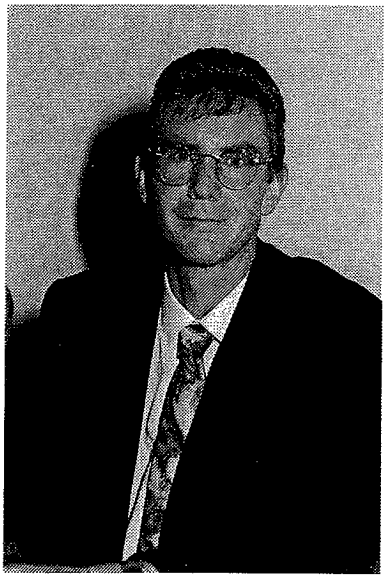
MAGNETIC RESONANCE IMAGING OF BLOOD FLOW VELOCITIES AND ANGIOGRAPHY OF THE CORONARY ARTERIES



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Magnetic Resonance Imaging of Blood Flow Velocities and Angiography of the Coronary Arteries

It is a great honour for me to have the opportunity to talk to you on this occasion and present my work. I am deeply indebted to the Latsis family, and to the evaluation commission for the recognition of my research work.

I am glad to present here the key parts of my work under the title "Magnetic Resonance Imaging of Blood Flow Velocities and Angiography of the Coronary Arteries". The presentation will deal with the application of magnetic resonance imaging to medical diagnosis. After its discovery in 1946 by the Nobel prize winners Felix Bloch and Edward Purcell, nuclear magnetic resonance was soon further developed both theoretically and methodologically by a number of groups, including namely Zürich's Nobel prize winner Richard Ernst. Developments to spatially encode magnetic resonance signals in the 1970's opened the way into the medical field.

Magnetic resonance imaging, or often abbreviated as MR, is an increasingly popular technique in medical diagnosis. It offers a superb soft tissue contrast, while being a fully non-invasive modality. No ionizing radiation is used, and with toady's MR equipment, there are no known adverse effects. It provides highly detailed anatomical information, which is shown with a high resolution brain image; but on top of that, more and more applications evolve to gain functional information. On the other hand, disadvantages are the relatively long examination times in the order of half an hour, which makes MR images susceptible to artefacts caused by patient motion and blood flow.

Blood Flow Velocity Measurements

One example of functional information derived from magnetic resonance images is the possibility to measure and quantitate blood flow velocities in human blood vessels based on a motion induced phase shift. Assuming that spins in blood move in direction of a magnetic field gradient, thus move from a region of lower towards a region of higher magnetic field, their precession frequency increases due to the increasing field. After a certain time the moving spins have accumulated a phase shift with respect to stationary spins. This effect is proportional to the velocity of the blood, and therefore provides a direct measurement of blood flow velocity. Images of the phase of the signal can be used for the visualization of only moving material. In the shown example, the blood vessels in the neck, which supply the head and brain, are visible.

In conventional magnetic resonance imaging techniques, after the excitation of spins with a radiofrequency pulse, the magnetic resonance signal is sampled during the application of a field gradient to provide a spatial encoding. The acquisition of what we call here a 'full echo' provides data containing easily accessible phase information, and this phase of the MR signal carries information about the blood flow velocities. However, the acquisition of a full echo leads to a relatively long time delay between the excitation of spins and the acquisition. This time delay, called *echo time* is usually in the order of 12 to 15 ms. If blood flow velocities vary over the time course of an imaging experiment, the sequences with long echo times are susceptible to artefacts caused by the blood moving with varying velocity.

The echo time can be shortened considerably down to about 4 ms, if only half of an echo signal is acquired, reducing the amount of flow artefacts to a large degree. Images from pulsatile flow in a

Y-bifurcation model, which are acquired with full echo data acquisition and an echo time of 14 ms show a high flow artefact level, making flow measurements nearly impossible, whereas images acquired with our half echo time sequence and a corresponding echo time of only 4.5 ms exhibit negligible artefacts. However, half echo signals are susceptible to system imperfections, and the phase information is not easily usable to yield blood velocity measurements.

My proposal to gain flow information with half echo sequences and corresponding low artefact level is to acquire two half echos in two separate measurements. In the second measurement the sign of the field gradient applied during the acquisition of the MR signal is reversed with respect to the first measurement. Thus, the 'left' and the 'right' halves of a full echo are measured separately, both with very short echo time. These signal parts are then later on combined in a computer to form a full echo. The proposed acquisition technique is now being used for quantitative flow measurements in several hospitals in Europe. The blood flow velocities in the abdominal aorta on the level of the truncus coeliacus of a healthy person are shown. Data of the pulsatile blood flow are presented as grid plots with measurements every 30 ms during the heart beat cycle. During systole, the contraction phase of the heart, high forward blood flow is seen with maximum velocities in the range of 1.2 meters per second. An interesting fact is the abrupt reversal of flow, caused by the reflection of the pulse wave in peripheral vessels, which, and this is visible on the profile in front, occurs initially in the posterolateral part of the aorta, and later on over the whole cross sectional area.

In regions of vessel bifurcations blood does not uniformly flow in the direction of the vessel, but rather complicated flow patterns can be observed. This is underlined with blood flow measurements in the bifurcation of the carotid artery. Flow patterns parallel and

perpendicular to the vessel direction are presented, and secondary flow patterns are visible. One particular application of magnetic resonance blood velocity measurements with high spatial resolution is research to gain more insight in the onset and development of arteriosclerotic disease. Recent results support the theory that fibrotic plaque, and later on vessel occlusion occur predominantly in areas with low wall shear stress, and in recirculation zones with long residence times of blood particles. Exact measurements of three dimensional velocity patterns in both normal and diseased human arteries may contribute towards a better understanding of the development of vascular lesions.

MR Imaging of the Coronary Arteries

There is a second possibility to distinguish static tissue from moving blood, and this brings us to the second part of the presentation. A selected slice is excited with radiofrequency pulses very rapidly, for instance every 20 ms, and spins within the slice are saturated and little signal can be gained. In blood vessels however, fresh blood with unsaturated spins flows into the slice during the experiment. These fresh spins have not seen previous excitations, and consequently contribute a high signal. This "inflow" effect can be exploited to image almost exclusively blood vessels. In the brain, the technique provides fine details of small blood vessels down to a vessel diameter of less than one millimeter.

Cardiovascular diseases, and in particular diseases of the vessels supplying the heart muscle, the coronary arteries, are still a major cause of mortality in the industrialized western world. There exists one clinically widely used modality to image the coronary anatomy, X-ray contrast angiography. However, this technique has some drawbacks. Mainly it is invasive, a contrast agent is delivered with a catheter directly into the artery, and X-ray projection images are taken. The procedure is rather expensive, and, due to the invasive

nature, is associated with a small risk. Therefore, a fully noninvasive visualization of the coronary arteries would be a highly useful tool, and represent a step towards better patient comfort.

Since there is such a need for noninvasive coronary angiography, there have been early attempts with magnetic resonance imaging, but with moderate success. There are a number of problems, centered mainly around the low resolution of MR images in the heart, and the artefacts caused by the respiratory motion of the heart. We acquire the MR signals with a dedicated heart receive coil which picks up signals only from the heart, and thus an image resolution of less than 1 x 1 millimeter with 2 millimeter thick slices is achieved. A large number of slices is acquired in a linear fashion to image the whole heart in a three dimensional data set. Adjacent slices overlap each other, and this slice overlap creates an inflow effect; the signals of the coronary arteries are larger than those from surrounding myocardial tissue or fat. After end-systole, the first slice is measured at an apical level (the tip of the heart). During diastole the imaged slice moves up towards the base of the heart, until, at the end of diastole, the last slice is imaged at the level of the ascending aorta.

Coronary arteries are displaced several centimeters during a respiration cycle, so it is absolutely necessary, that the patient holds his breath during data acquisition. The data acquisition for MR images however, lasts several minutes, too long for the patient to hold his breath. Therefore, we propose that the patient has to follow a breathing scheme: The scheme is very easy to follow, since it resembles closely normal breathing, and no breath-holds are required. After exhalation, the patient waits approximately 2 seconds, and during this time data are measured. This procedure is repeated 170 times for totally about 10 minutes.

Coronary arteries, and this is true for younger as well as older persons, are mostly surrounded by fat. Therefore, for good image contrast, the suppression of MR signals from fat tissue is a key issue. We therefore use fat saturation pulses which selectively excite and spoil the signal from fat tissue. Since such a pulse lasts 15 ms, we apply only one fat suppression pulse per 100 milliseconds imaging time. This results in a large reduction of the signals from fat, and the image contrast in the coronary vessels is greatly enhanced. A single MR image is presented in which the left main coronary artery and a longer segment of the left anterior descending coronary artery is visible.

Usually 30 to 60 image slices are obtained, with only a small part of a coronary artery in each single image. In order to bring this large amount of information into a presentable form, the coronary vessels are segmented semi-automatically on a computer workstation, and then displayed as three-dimensional objects, which can be rotated into any desired view.

Such a 3-dimensional reconstruction from a patient is presented, with an MR examination 4 months after the treatment of a high grade coronary lesion with percutaneous transluminal coronary angioplasty. Unfortunately, in a certain number of patients vessels in the treated location narrow again, exactly what happened in this case. In another patient a very tight coronary stenosis was found, and in the MR examination performed one day after the treatment, the vessel was perfectly open, showing the successful intervention. In follow-up examinations 3 and 6 months later the vessel remained stable, and no narrowing was discovered. This demonstrates the usefulness of the method for monitoring patients likely to develop such a restenosis.

Of course the procedure needs to be validated. This was done comparing the diameter of the coronary arteries as measured with magnetic resonance and with the invasive X-ray technique. The correlation of measured coronary diameters across 10 patients and almost 50 measurement points was good, with a correlation coefficient of 0.76. The mean difference between measurements was only 0.2 millimeters.

So where do we stand now? In a series of patient examinations 82% of the coronary artery lesions could be identified correctly with magnetic resonance. The comparison of vessel diameters showed that the magnetic resonance images matched well with the results of the conventional invasive technique. However, this was true only for diameters in healthy normal segments, the diameters in diseased locations could not be measured reliably, there was always some signal loss leading to an overestimation of the narrowing.

So as a conclusion for the time being it can be said that follow-up examinations after interventions for the treatment of coronary artery disease are possible non-invasively with magnetic resonance imaging. For the direct diagnosis of this disease however, the MR-technique needs further improvements, until it can be reliably used in clinical routine. And, both with the invasive X-ray contrast angiography as well as with magnetic resonance imaging, purely anatomical information is obtained, and the physiological significance of the lesion, i.e. what are the effects of a particular stenosis, is not addressed.

Current Developments

This brings us to current research in our laboratory which goes mainly in two directions: Firstly, we are currently working on better monitoring of the breathing motion to further reduce the artefacts from patient breathing.

Another topic, and this leads us back to flow measurements, is the fact that the physiologic significance of a lesion can be quantitated with the measurement of the remaining blood that flows through a narrowed blood vessel.

This is work from one of my collaborators, Gerard Crelier. With magnetic resonance, spins of a single well defined slice are usually excited. With more sophisticated excitation pulses the spins in only a selected cylinder can be measured very rapidly. Using such a cylinder excitation technique we measure the motion of the diaphragm next to the heart. So, rather than possibly inaccurate external motion sensors, magnetic resonance itself can be used to precisely locate the position of the heart, and thus trigger and guide the data acquisition for the MR images. This triggering mechanism is believed to deliver an improved image resolution in the coronary arteries, and further reduce breathing motion artefacts.

Coronary flow was measured and quantitated at 10 to 12 time points across the heart beat cycle. Video sequences of MR images show the rapid movement of the small coronary arteries with the beating heart. Preliminary measurements in young volunteers exhibit the expected blood flow pattern, i.e. low blood flow in the coronary arteries during systole, and the predominant blood supply of the myocardial muscle during diastolic relaxation. Such measurements are hoped to yield information beyond the pure vascular anatomy. Quantitative functional information is expected, on whether the disease of a vessel segment in a particular patient is significant, and whether there is a potential danger to this patient for a sudden myocardial infarct.

Finally, I wish to mention and thank all my direct collaborators in our research team, which contributed to work presented here. I would like to mention in particular, Stefan Fischer, Gerard Crelier,

who developed the pulses for the cylinder excitation, Matthias Stuber, and René Botnar, who performed some blood flow measurements in the carotid arteries.

Of course I want to thank Professor Bösiger, head of our magnetic resonance research team, and Professor Anliker, head of the Institute of Biomedical Technology, and Medical Informatics. Both provided me with a very exciting work environment, and made these developments possible.

Again, I express my deep gratitude towards the Latsis Foundation, and, ladies and gentlemen, thank you very much for your attention.