SPECIAL

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Magnetic Resonance Imaging special

Women's & Men's Health: Breast & Prostate Imaging

Interviews with Toshiba Medical's Users

Green Apple Award for Vantage Elan

TOSHIBA MEDICAL

VISIONS Special:
Magnetic Resonance Imaging

Publisher
Toshiba Medical Systems Europe B.V.
Zilverstraat 1
NL-2718 RP Zoetermeer
Tel.: +31 79 368 92 22
Fax: +31 79 368 94 44
Web: www.toshiba-medical.eu
Email: visions@toshiba-medical.eu

Editor-in-chief
Jack Hoogendoorn (jack.hoogendoorn@toshiba-medical.eu)

Editor
Jacqueline de Graaf (jacqueline.degraaf@toshiba-medical.eu)

Modality coordinator and reviewer MRI
Martin de Jong

Design & Layout
Boerma Reclame (www.boermareclame.com)

Printmanagement
Het Staat Gedrukt (www.hetstaatgedrukt.nl)

Text contributions and editing
The Creative Practice (www.thecreativepractice.com)

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Dear reader,

In your hands you have a new and special edition of our VISIONS magazine, totally dedicated to Magnetic Resonance Imaging. You will find articles about many recent achievements, upcoming events and product developments. Please let me walk you through: The MRI products in our portfolio have been updated with the latest M-Power 4.0 'Zen Edition' software. They are now applicable for all MR models, including our latest system, the Vantage Galan 3T. Customers can benefit from new applications via hard- and software upgrades from existing platforms. Find out more about the Zen Edition features in this Special.

Innovation has always been a top priority in MRI development at Toshiba Medical. The history of MRI in general has always featured important scientific innovations developed by researchers and scientists from the world's leading universities. Many of these achievements are highly recognized: a total of nine Nobel Prizes have been awarded in this field. One of the first was the Nobel Prize awarded in 1952 to Felix Bloch and Edward Mills Purcell for their development of new methods for nuclear precision measurements and discoveries in connection with these methods. This was the world's first Spin Echo experiment. One of the most well-known in this field, however, is the Nobel Prize awarded to Sir Peter Mansfield and Paul Lauterbur in 2003 for discoveries with MR Imaging that describe the application of a field gradient to decode the spin localization.

Alongside this, Toshiba Medical has established long-term customer research collaborations with some of the world's leading academic partners, such as Kyoto University, Japan; John Hopkin's University, Baltimore and the University of California (UCSD), San Diego, USA. We are very proud to have them as research partners.

Toshiba Medical recently started a new partnership in Europe with Prof. Vincent Dousset at the University of Bordeaux, France. Working together with his team on research and development projects, for sure we will advance technologies in Neuroradiology. And we also look forward to working with Prof. Luca Saba from the University of Cagliari, on Sardinia, Italy from the beginning of 2018 onwards. More information will follow soon.

In addition to collaborations with scientific groups, Toshiba Medical also works with leading sports organizations and is Official Medical Systems Partner to some of the world's top football clubs, including Manchester United, FC Barcelona and Real Madrid. These collaborations not only demonstrate our leadership in MSK imaging, but have also enabled the start-up of joint research projects that hold the potential to optimize the performance of elite athletes, advance diagnostics, and improve treatment strategies of injuries. This knowledge can then be transferred and translated into applications and innovations in other sports environments. These include a Muscle Talent Study, cardiac screening for young players, and more.
Together with our friends at Olea Medical, we look forward to continuing and extending our scientific collaborations further in the interest of all our customers. We all will benefit from more advanced and unique applications to improve the quality of life of patients according to our company's vision: *'Made for Life'*.

Kind regards,

Dirk Berneking
Business Unit Manager MRI Europe
Toshiba Medical Systems Europe BV

To download the digital version
of this MRI special, visit:
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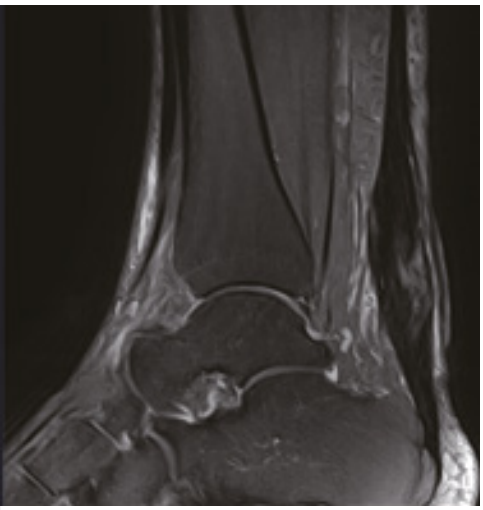
MADE FOR LIFE CAMPAIGN



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At the Forefront of Diagnostic Imaging with the Vantage Galan 3T

As interest in the Vantage Galan™ 3T MRI system grows since its launch in November 2016, the system is already in use by some of Europe's leading imaging experts. VISIONS magazine finds out what Professor Martin Zwaan, Head of the Institute for Diagnostic and Interventional Radiology (DIR) at the Ammerland Klinik in Westerstede (Germany), and Dr Xavier Alomar, Head of Radiology at The Clinica Creu Blanca (Spain), think of the new MRI system.

Impressive Image Quality

Combining wide coverage (max. 50 x 50 x 205 cm) and visualization of the smallest details, by virtue of up to 128 HF channels, the image quality achievable with the Vantage Galan 3T appealed to both physicians.

"My aim is to have the best image quality possible. New applications are explored with the latest developed sequences." Dr. Alomar said. "With the Vantage Galan 3T, Toshiba Medical has now a real competitive product offer in this market."

"We have found the Vantage Galan 3T amazingly good for examination of joints and the head, with hardly any artefacts. I don't know if the others have the same results, but it is very impressive!" added Prof. Zwaan. "Double Inversion Recovery with the system is really, really good. It's much clearer. It shortens the time that the Radiologist needs to diagnose a patient's condition."

Combining active- and passive shimming, the Vantage Galan 3T's compact and light magnet achieves a very stable magnetic field with a high degree of homogeneity. This ensures excellent imaging in whole body scans. Furthermore, the outstanding homogeneity in the large cylindrical field of view (50 x 50 x 45 cm) ensures very high accuracy of detail, even in the off-center field of view (e.g. shoulder and full abdomen). At the same time, this provides excellent fat-water separation; spectral fat saturation is of extraordinary quality, even at the edges of the field of view. As a result, the Vantage Galan 3T achieves outstanding measurements in spectroscopic scans. In addition, new RF technology, combined with the Saturn gradients, improves signal-noise ratio by up to 20%.

Advanced Software

In addition to generous standard features, such as a variety of non-contrast sequences, 3D post-processing and many more advanced packages are available. Olea Nova+ is an example (currently a research application that may drastically reduce measurement time), which extends the spectrum of imaging with

Prof. Martin Zwaan, *Head of the Institute for Diagnostic and Interventional Radiology, The Ammerland Klinik, Westerstede, Germany.*

Dr. Xavier Alomar, *Head of Radiology, Clinica Creu Blanca, Barcelona, Spain.*

the Vantage Galan 3T even further. Both Prof. Zwaan and Dr. Alomar have worked with Toshiba Medical on development of Nova+ together with Olea Medical.

"We are working together with Toshiba Medical on stability and innovation. We are very happy with this collaboration and happy that we can explain what we need to the development team" said Dr. Alomar. "In particular, we think that Olea Nova+ is a new and particularly promising technique for MRI that can add value to normal clinical scanning. I think concepts in MRI will change significantly in the next few years. Computed MRI could replace much of the regular clinical scanning, for example. And I think we will be differentiating more various types of tumors using different sequences."

Non-Contrast Applications

New sequences are also available with the Vantage Galan 3T, such as those for coronary artery imaging without contrast medium, 4D MRA of the brain and many other examinations. Two points predominate the discussion on contrast agents. Firstly, it is not possible to use a contrast medium in patients with poor renal function. And secondly, many physicians and researchers question the breakdown of some of the contrast media within the body.

"The Vantage Galan 3T system is very convenient from the perspective of the variety of examinations that we can carry out without contrast medium," Prof. Zwaan remarked. "We try to minimize the use of contrast agents as far as possible. If there is a requirement to use a contrast agent, only macrocyclic contrast agents are used, with exception of Primovist for liver investigations.

In examinations of the lower leg it is sometimes difficult to display both legs, due to differences in flow velocity of the blood. Therefore it's a big advantage to have more time-resolved sequences available, to display the correct phase in each leg. With a contrast-free sequence, scans can be repeated indefinitely if required. In addition, if we are able to perform Gadolinium-free angiographies, it's a big advantage."

While many non-contrast sequences are available with the Vantage Galan 3T, Dr. Alomar currently still uses contrast agents in several clinical applications.

"Gadolinium based contrast agents are used as they provide specific information for a correct diagnose. Of course, if recommendations say that Gadolinium should not be used, we will do so, although this is not the case at this moment." Dr. Alomar remarked. "I think in the future, new sequences will enable better characterization, so contrast agents will not be necessary, but at this moment the contrast is important for our clinical applications."

Research Interests

As a recognized stroke, Multiple Sclerosis (MS) and Neuromuscular Disease center, with 60 beds dedicated to neurological patients, the Ammerland Klinik is one of the biggest centers of expertise in Neurology in North West Germany. Therefore, brain imaging with the Vantage Galan 3T system, is a key research field at the Clinic.

"We are profiling patients with healthy brains and those with Alzheimer's disease and Multiple Sclerosis. With these images, we are working in cooperation with a local firm (that has evolved from university research origins) to build volumetric profiles of the brain with the aim of identifying new volumetric standards of the brain. They create these profiles based on MPRAGE data, which is produced with the Vantage Galan 3T. It contains all required information for this reserach project. The eventual results of the study will be available for all," explained Prof. Zwaan.

"What we would be very interested in for the future is using the Vantage Galan 3T in combination with a neuro-CT. This would be amazing for our work using Brainlab software. The issue is that once you open the skull during surgery, the brain deforms to some degree because some CSF (Cerbro Spinal Fluid) is lost. Combining information from different modalities can help."

Involved also in computed MRI research for imaging of the joints, as well as brain imaging, the Ammerland Klinik hopes that this will have even more widespread application in the future.

"With a little more success in these fields, we would try this for prostate imaging," added Prof. Zwaan. "This is, however, a difficult area with more movement and a contrast medium is always required. We don't have much previous experience with using this system in studies in prostate patients, but as we are making huge progress with the Vantage Galan 3T in other fields, this would be a logical step forward."

"I am currently working with 3T in the hip area, on muscle injuries, the knee, ankle and hand. 3T scanning is also important for brain diagnoses," remarked Dr. Alomar. "And we have just started to use the Vantage Galan 3T with 16 channel flex coils for studies

in prostatic cancer. The image quality is excellent. I am very happy with the diffusion and also the T2W images are very good. In anterior/posterior the image quality is very good. The protocols that we have tried give a superior image quality and we will introduce this as standard. The key in my opinion is the specific use of 16 channel flex coils."

Inside the new Vantage Galan 3T, the improved gradient coils in Saturn quality, ensure top performance capacity with diagnostic accuracy and the highest standard of image quality. The system works with an improved version of the 'tried and trusted', Vantage Series matrix coil concept and new, second-generation, ATLAS coils. They are particularly well-adapted to local anatomy, but can also be combined when examining larger areas.

Future Prospects

Prof. Zwaan anticipates even faster scanning capabilities in the future for non-contrast angiograms. He also believes that computed MRI, introduced as Olea Nova+ by Toshiba and Olea, could have clinical relevance in the trauma department. It could be particularly useful with young patients, as a possible replacement for a CT, to quickly perform a diagnose without radiation.

"We are very satisfied with our Vantage Galan 3T and its outstanding image quality. I would recommend this system for neurological and orthopedic diagnosis and treatment planning. The system opens up new dimensions in sectional image diagnostics and especially in our clinic, the neuro-diagnostics, which can be treated quickly by interventions. With its new clinical innovation, Olea Nova+, we are discovering possibilities that will take us in a new direction in the future."

"With the Vantage Galan 3T, we are discovering new possibilities."

Prof. Martin Zwaan, *Head of the Institute for Diagnostic and Interventional Radiology, The Ammerland Klinik, Westerstede, Germany.*

Regional Hospital

The Ammerland Klinik is a general regional hospital, in Westerstede, near Bremen, Germany. With expertise in treatment of neurological and vascular conditions, it has emerged as one of the biggest Interventional Radiology centers in Germany. Prof. Martin Zwaan is the Head of the Institute for Diagnostic and Interventional Radiology that recently acquired the hospital's first 3T MRI scanner - the Vantage Galan 3T. With the new system, the radiology team can advance its existing specialist work and expand its research in other diagnostic areas, as well as reduce patient waiting times for high-end MRI scans.

Almost 10 years ago, the Ammerland Klinik combined military and civilian medical facilities. The large Radiology team at the hospital now comprises five military physicians and 12 civilian physicians, who work very closely together as one department. Prof. Zwaan heads the Institute for Diagnostic and Interventional Radiology. Alongside he specializes in vascular imaging and interventions.

"As a hospital with several specialities including neuro- and vascular surgery, we were interested to acquire the Vantage Galan 3T to complement our 1.5T MRI system," said Prof. Zwaan. "We are particularly interested in imaging of vessels and, in particular, the contrast-free imaging of vessels, because a lot of our patients with peripheral arterial disease are diabetic and have decreased renal function, therefore, we need to make many studies without contrast media in our diagnostics. In addition, we have a lot of trauma patients, and therefore a high demand for joint imaging, because the Clinic is also a trauma center run in conjunction with the German Armed Forces."

"I am very happy with the Vantage Galan 3T with its new software," he concluded. "Follow up from the Toshiba Medical team is good and we are able to work with new sequences on the system."

Dr. Alomar and his team are working closely together with Toshiba Medical on advancing clinical applications with the Vantage Galan 3T.

"My aim is to have the best image quality."

Private Diagnostic Clinic

The Clinica Creu Blanca, is a large, private diagnostic clinic in Barcelona, Spain. Well known for applying the very latest innovations in diagnostics, the clinic provides diagnostic services to private insurance companies and private doctors. Head of Radiology, Dr. Xavier Alomar is globally recognized as an expert in musculoskeletal (MSK) MRI. He has carried out a wide range of research in this field, including studies that have contributed to improving sports medicine and elite sports in conjunction with top sports clubs, such as FC Barcelona. While he has used 3T MRI for several years, Dr. Alomar explains how the Clinic's new Vantage Galan 3T enables advanced techniques in MSK, neurological and prostate imaging.

The Clinica Creu Blanca belongs to the Creu Blanca diagnostic group, which has four clinics in Barcelona and two in Aragon. The group provides a wide range of diagnostic medical services, with follow up and treatment carried out externally. Using cutting edge techniques, Dr. Alomar's work is dedicated to driving diagnostic imaging forward.

"My role is to find new possibilities in diagnostic imaging," said Dr. Alomar. "I look for new sequences, apply these in clinical applications and introduce them in our field of expertise. Quality and advanced applications enable progress. It is about continuous development."

Dr. Xavier Alomar, *Head of Radiology, Clinica Creu Blanca, Barcelona, Spain.*

Vantage Titan 3T -

Pushing the Boundaries in Neurovascular Imaging

Dr. Andreas Schilling

Dr. Andreas Schilling is Head of the Radiology Department at Klinikum Frankfurt (Oder, Germany). Together with his team, he is exploring new avenues in the treatment of arteriovenous malformations.

More than 75,000 patients from Frankfurt (Oder) and its region are treated in the Klinikum. The treatment of vascular diseases in the brain, as well as tumorous diseases and injuries in the brain, are specialist fields for the clinic. There are only a handful specialized centres for this specific disease field. Since October 2015, Klinikum Frankfurt has been the only hospital in Germany to have a Toshiba Medical Vantage Titan™ 3T MRI Scanner. The device is used by the hospital primarily to investigate cerebral arteriovenous malformations. Thanks to three-dimensional depiction and visibility in layers over the course of time, possible with the Vantage Titan 3T, traditional angiography via X-ray images will be replaced in the future . The overall advantage is the reduction of radiation load to zero, also the intervention has fewer risks and the MRI Images show the surrounding brain tissue.

MRI scans are predominantly used as an additional source of information in the diagnosis of arteriovenous malformations (i.e. short circuits, as it could be envisaged, between arteries and veins that may lead to epilepsy or hemorrhages, amongst other things). The traditional X-ray angiography is still the gold standard. The reason for this is that it has not been possible to date to obtain adequate information from the MRI regarding perfusion of the arteries. "The image acquisition speed in a standard MRI is not fast enough," explained Radiologist, Dr. Andreas Schilling. "Being able to see the flow velocity effectively in the moving image, however, is exceptionally important for me. I need to know whether I have successfully reduced the blood flow as a result of an intervention, and whether the patient is safe from a risk of hemorrhage." On the other hand, MRI scans also have a significant advantage over traditional angiography with X-ray imaging. They enable us to easily obtain a three-dimensional layer model of vascular changes in the brain, even without contrast medium, which is required in X-ray imaging. Three-dimensional visualisation is a huge help, as vascular changes often appear as unclear knots of arteries.

Dr. Schilling has been using a Vantage Titan 3T in his clinic since last summer. "We have selected a Toshiba Medical MRI system, as this system is optimized for the depiction of vessels. This is a natural fit for a clinic such as ours with a neurovascular specialism," he explained. His goal is to switch to MRI entirely in the future, not just for diagnosis and treatment planning, but also for real-time imaging during surgery. "At the moment, we stand at an image per second in an MRI, using the best technology that is currently on the market. In the X-ray procedure, it is six images per second. We need a spatial resolution of at least half a millimeter for six images per second. Today, the MRI gives us an accuracy of two millimeters with an image speed of one image per second."

In consultation with the developers at Toshiba Medical, Dr. Andreas Schilling and his team are working on gradually improving the vascular MRI sequences. "We explain our requirements to the developpers and they explain what is possible at this moment in time. On a regular base we receive updates based on our requirements." Optimisation occurs entirely at software level. "There is actually nothing more in terms of hardware that we could purchase," said Dr. Schilling.

From a purely practical point of view, the treatment of arteriovenous malformations using the MRI scanner would be entirely possible. When the patient's head is placed in the center of the magnet, the groin still protrudes. The catheter through which the procedure in the brain is carried out is inserted here. Obviously there are problems that still need to be solved. Dr. Schilling explained: "We currently use a small gold ring as marking for the microcatheter. And to bring the catheter in to where it should be, we use a guide wire. Both of these would lead to artefacts in an MRI. All that would have to be rethought, but I feel that it is feasible."

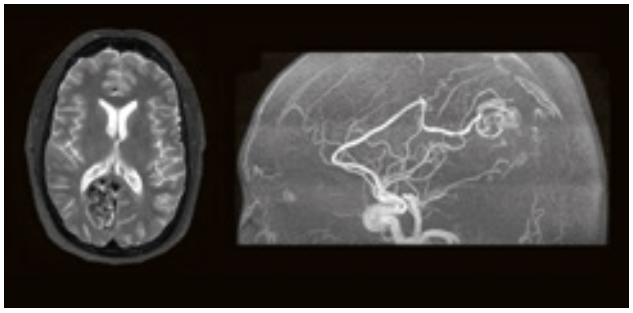

Figure 1: MR axial T2 and MRA of the head.

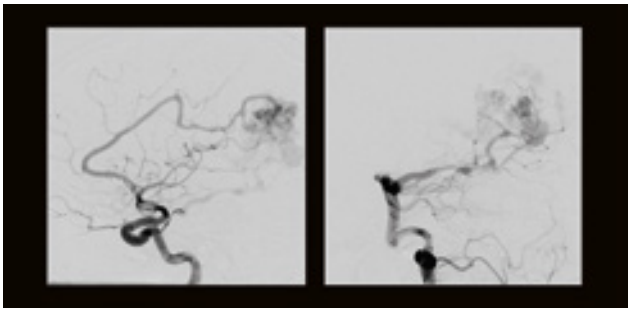

Figure 2: Conventional angiography of an AVM.

Dr. Andreas Schilling.

A significant advantage of switching from X-ray to MRI would be the discontinuation of exposure to radiation. This would not only benefit the patients, but also the doctors, who currently have to be clothed entirely in lead during the procedure. More importantly, MR angiography also shows brain tissue, contrary to X-ray imaging. It is possible to monitor how the brain reacts to an intervention in real time using MRI – something that at the moment can only be determined retrospectively in follow-up examinations. "We would also be better able to see if a microcatheter inadvertently damages a vessel wall and causes bleeding. In that case, I would know that I need to close it quickly, or even operate in an emergency. Or, if allergic reactions occur, medication can be administered to counteract them," explains Dr. Schilling.

Another hurdle that must be overcome during the intervention is the precise application of the adhesive with which the misdirecting artery is to be closed. The procedure has to be planned accurately so that the efferent vein is not bonded and the adhesive does not harden before it arrives at the correct position. In practical terms, this means that the adhesive mixture must be adapted to the flow velocity of the blood in the affected artery. Currently, we have to settle more or less for estimates. "However you could take objective flow measurements with an MRI," reasons Dr. Schilling said.

This is not all a dream for the future. Dr. Schilling and his team are already using MRI now to reduce the amount of X-ray imaging. On the MRI Image the pathway for the contrast agent filled catheter
can be detected easily and transfered to the X-ray. In an ideal scenario, you would only have to produce an X-ray image of the area of interest, and, would not have to first treat the surrounding vessels with a contrast medium and then X-ray them. "We currently still use traditional angiography in the surrounding areas. It can still happen that a turbulent flow in a vessel leads to the effect on the MRI image that the vessel is depicted to be thinner than it really is. However, these phenomena are well known and not surprises for us," explained Dr. Schilling.

Treatment under MRI monitoring would also be interesting for another clinical picture: aneurysmal bleeding. Three to four in every 100,000 people have an arteriovenous malformation (which is often not abnormal). Around 100 patients with arteriovenous malformation are treated annually in Frankfurt (Oder). An enlargement in the artery in the form of an aneurysm, however, is present in 8% of all people. One in ten cases leads to bleeding. That is 800 cases in a population of 100,000 people. A common treatment in the case of aneurysmal bleeding is what is called coiling: filling of the pathological bulge in the arterial wall with platinum spirals. During an intervention such as this, good spatial resolution in the

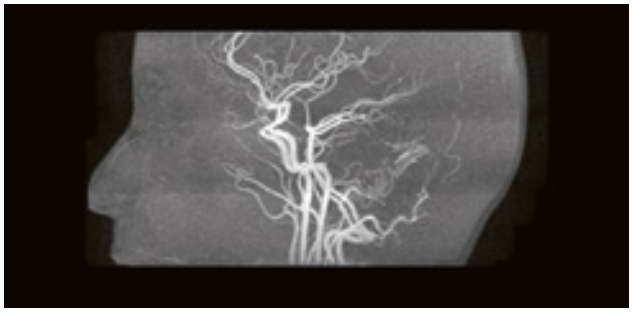

Figure 3: MRA of the head - diagnosis. Previous embolisation.

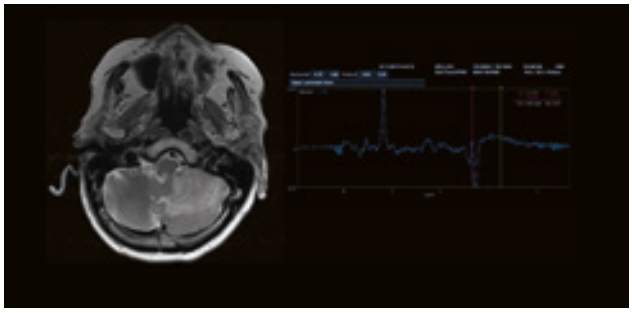

Figure 4: Spectroscopy.

imaging is required above everything else. The temporal sequencing is not so critical. Dr. Schilling believes that, in five years' time, MRI will be developed enough to replace X-ray imaging during coiling.

In addition to depiction over time, the Titan 3T facilitates an additional diagnostic process used in Frankfurt (Oder): Magnetic Resonance Spectroscopy (MRS). "Instead of generating an image of brain structures, you can also easily measure how frequently specific types of molecules that are involved in metabolism occur in the brain," explains Dr. Schilling. It is often not possible to detect if an abnormality involves an inflammation, an infarction or something else, using angiography alone. Using the molecular markers, however, it can be decided whether the tissue is, for example, inflamed, or whether there is a tumor, and if this is benign or malignant and slow- or fast-growing.

"A creatinine peak, for example, indicates high cell division activity. A reduced choline level indicates a low energy level. N-acetylaspartate shows how much brain tissue is present. Lactate and lipid peaks indicate pathological symptoms."

The analysis procedure can be carried out for individual areas of the brain separately. "If there is a structure in the brain and I do not know what it is, that can be very helpful. I can help the neurosurgeons taking a sample at the best position: Better look to the front instead of the back, it looks more conspicuous. Or if there is a patient with symptoms of a stroke, who is actually too young to have a stroke. The spectroscopy provides indices if tumourcells are involved." The follow-up check after doses of radiotherapy is another possible application. Areas of inflammation or pseudo progression, which may occur following the treatment, cannot be diagnosed clearly by means of imaging. Magnetic Resonance Spectroscopy ultimately cannot fully replace other diagnostic procedures. However, like MR Angiography, it provides additional information in order to better plan invasive or radiation-intensive procedures in the diagnosis and treatment and, enable their reduction. //

Dr. Andreas Schilling
Head of the Radiology Department in Klinikum Frankfurt (Oder) Germany.

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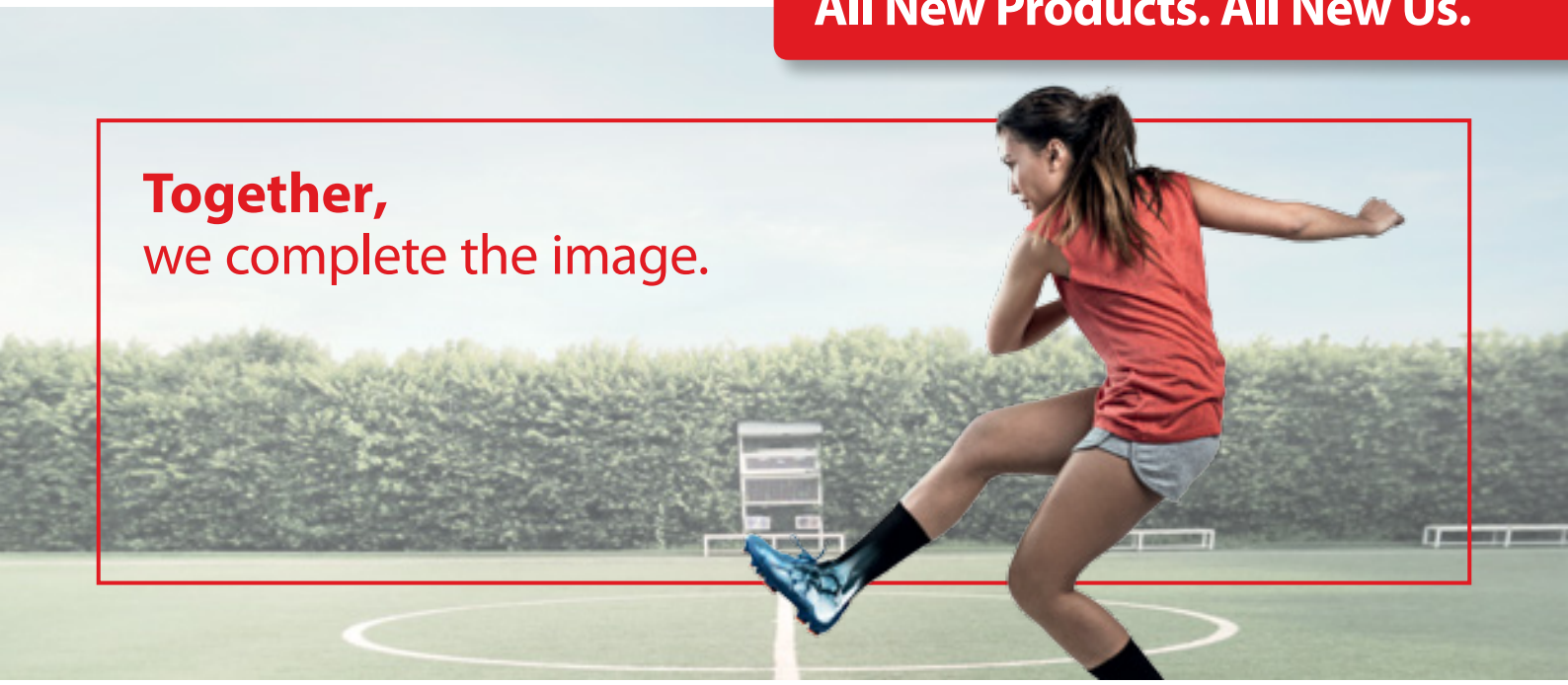

Toshiba Medical is now part of the Canon family. So the same source of abundant innovation and technology leadership today is supported by our committed new ownership.

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Toshiba Medical has been adding strength to strength. As part of the Canon group, we'll be even stronger.

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*Compared to filtered back projection (FBP) on the Aquilion ONE ViSION (TSX-301C) system.
The Infinix-i Sky + is the INFX-8000C with 930A C-arm.

Made For life

Toshiba Medical receives Green Apple Environment Award 2016

Toshiba Medical has received the prestigious Green Apple Award for its Vantage Elan™ MRI System. The Green Apple Award is a global recognition of innovation that contributes to environmental best practice.

On the right: Mark Holmshaw, President and CEO at Toshiba Medical Europe.

Specially designed to save space and energy, operate quietly, and provide optimal patient comfort along with top quality imaging capabilities, Toshiba Medical's Vantage Elan™ MRI scanner occupies a minimum footprint in hospitals and reduces power requirements by almost 70%.

"We are honored and delighted to receive this important award and consider it a token of appreciation for our ongoing efforts to reduce overall impact on the environment," said Mark Holmshaw, Toshiba Medical's President and CEO. "Toshiba Medical's commitment to the environment dates way back to 1975, when plans for an eco-friendly factory in Nasu, Japan were developed featuring a biological water-treatment and purification system. More than 40 years later, our commitment to the environment has intensified. We develop products that offer significant environmental benefits, while providing the best possible medical images to enable medical professionals to make better, faster and more accurate diagnoses for patients, as well as enhanced comfort."

The Vantage Elan MRI scanner features a wide variety of advanced technologies that enable it to deliver outstanding clinical, environmental and economic benefits.

Significantly Reduced Footprint

The new, mobile Vantage Elan MRI scanner has the smallest-in-class installation space (approximately 23 m^2), but offers patients and clinicians almost 50% more inside space than conventional mobile MRI units. However, at just 3.5m wide, it does not require a separate escort vehicle during transportation. In addition, thanks to a unique loading and unloading mechanism, it can be relocated quickly and easily.

The scanner achieves lowest-in-class power consumption of 25 kVA through the combination of a small-capacity power supply, Zero Helium Boil-Off System and ECO Mode technology, which minimizes system operating costs, with power consumption dramatically reduced when the system is idle. Power requirements for the Vantage Elan are approximately one third less than that for other models.

A Quiet MRI for Every Sequence, Scan and Patient

Acoustic noise from equipment is a potential nuisance for both patients and medical staff. Toshiba Medical's patented Pianissimo technology, which was first introduced in 1999, dramatically reduces the noise in and around the MRI environment, making examinations more comfortable and easier to complete.

The Vantage Elan MRI scanner features a 1.4m ultra-short magnet with excellent magnetic field homogeneity, which ensures ultra high image quality, while ensuring more comfortable examinations and reducing patient anxiety. It is ideal for

What are The Green Apple Awards?

Green Apple Awards are a prestigious global recognition of environmental best practice issued by The Green Organisation - an international, independent, non-profit, non-political, non-activist environment group that was established in 1994 to recognize, reward and promote environmental best practice around the world.

patients who may be more vulnerable to, or concerned about, the effects of radiation from X-Ray or CT examinations, or those who experience claustrophobia during the examination procedure. The accuracy of the scanner contributes to faster examination times, early detection of abnormalities, and reduction of radiation exposure to technicians and patients.

Improved Workflows

Toshiba Medical's commitment to producing reliable systems that offer maximum uptime, ensure increased utility and improved workflow for the lifetime of the Vantage Elan MRI scanner. //

Environmental Profile: Vantage Elan MRI Scanner

Space:
- Compact (approximately 23 m² installation space).
- Almost 50% more inner space than conventional mobile MRI units.
- 3.5m wide - no need for a separate escort vehicle during transportation.
- Maneuverable and easy to relocate.

Power:
- Low power requirement of 25kVA.
- Reduces power requirements by almost 70%.

CO_2:
- 12.7 ton/year - entire product life-cycle.
- 9.5 ton/year in use.

Noise:
- Reduces MR noise from the source by up to 90%.
- Point: Noise level < Environmental noise + 2dB.

Resources:
- 5.6% reduction in product mass.
- 48% reduction in packaging materials.

Musculoskeletal MRI in Football Medicine – essential, useful or too much information?

Dr Steve McNally

In the higher echelons of professional football, where financial resources are greater, the use of MRI as a diagnostic aid has been prevalent for the past 20 years. However, it has not always been employed as part of a validated clinical process with scans being requested sometimes for political reasons or simply in response to player/coach demand. The potential ramifications of MRI findings can go far beyond clinical management and affect transfer fees, player asset value, contract terms and conditions, insurability and medicolegal matters.

Radiologists reporting 'abnormal' findings can have detrimental effects on player wellbeing or confidence (or that of his/her therapist) leading to over-caution in training or rehabilitation and subsequent reduction in performance or athletic development. Clinical experience and scientific research show that many such 'abnormal' findings are in fact adaptive or developmental in response to the physical and biomechanical stresses of the sport and whilst they need to be recorded and noted once a player has been subjected to MRI examination, the interpretation by the referring practitioner is key as is subsequent communication to the player.

When interpreted within context by experienced sports physicians, therapists and radiologists working as a team, MRI can add great value if applied at appropriate times and situations as an adjunct alongside good clinical management. The advent of newer MRI techniques has increased diagnostic and screening/profiling possibilities and the development of functionally relevant protocols and sequences could enhance player care even further. Caution will be needed in how imaging information may be interpreted and potentially misused by those with business interests rather than patient welfare. This article will give an overview of musculoskeletal MRI as utilised in professional football though MRI is also becoming more widely used in the assessment of players from a cardiological and neurological perspective.

Clinical Relevance

Injury diagnosis

The majority of clinicians in professional football will not refer a player for MRI in the early stages of injury assessment partly because it is unlikely to change their immediate clinical management and also because their budgetary resources will not permit it. Amateur and recreational players are only likely to be referred for MRI if they have a significant injury and have been referred on to secondary care specialists such as orthopaedic surgeons.

Conversely, at top professional levels there is often increased pressure from the player and the manager/coach to give an immediate prognosis for an injury ('when will I be back, Doc?') and MRI has become fashionable as having a key role in that diagnostic and prognostic decision-making process. I have experienced situations where players have demanded a scan within minutes of leaving the pitch with muscle pain and whilst there are some infrequent indications for early MRI following a significant trauma it is often

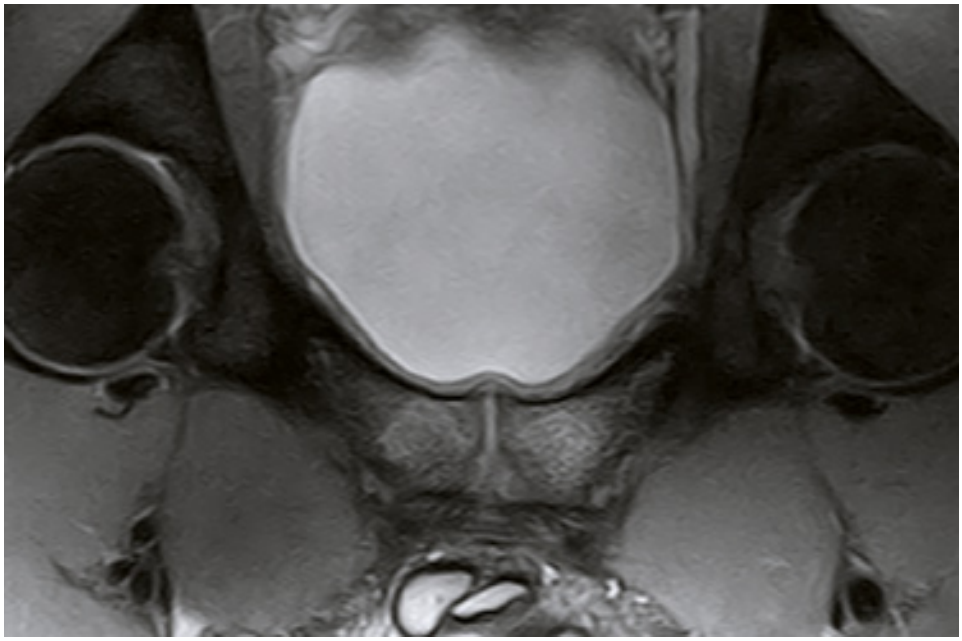

Figure 1: Coronal oblique PD FS image of a 17 year old footballer's pelvis showing typical functional stress-related bone oedema in the pubic body bilaterally.

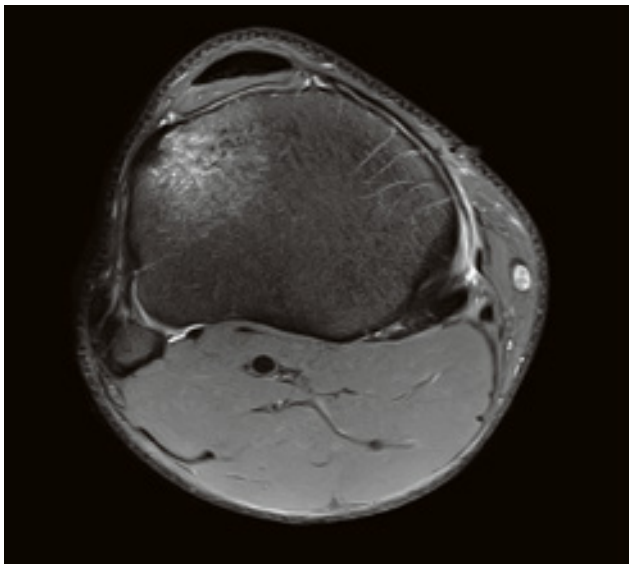

Figure 2: Axial PD FS image of a footballer's right knee showing a bony contusion in the medial proximal tibia due to a stud impact injury.

better to wait for the clinical picture to evolve and to allow the necessary physiological response to injury to occur in order that MRI can detect relevant pathological findings (oedema/haemorrhage, etc.). The timing and sequences applied will therefore depend on many factors such as player age, nature of trauma, time since trauma and suspected tissues involved. Player and coach education in these aspects is important as a means of managing the immediate situation which understandably causes anxiety in highly driven and motivated individuals who will be anxious about future results, performances, careers and the financial and personal implications of an injury. The more widespread use of ultrasound scanning by sports team physicians over recent years has been very helpful in appeasing players/coaches and in alleviating such anxieties whilst also being clinically useful as it is easily applied, relatively cheap and allows daily monitoring of injury evolution. MRI added to that combination at the right time with the right sequences and the right interpretation within context is often very valuable.

Joints (bone, cartilage ligament)

Traumatic injuries to the knee, ankle and midfoot joints are very common in football, predominantly in the form of ligament sprains/ruptures; overuse injuries can affect those joints but also the lumbar spine, hips and pubic symphysis. Shoulder, elbow and wrist injuries are less common but are often significant when present, including dislocations, subluxations, fractures and loose bodies. Whilst X-rays still play a role as the primary investigation for the suspected fracture and ultrasound can be of use in superficial bony and ligamentous lesions, MRI is the go-to modality for the complete assessment from an imaging perspective in joint injury, particularly if there is associated joint swelling (effusion or haemarthrosis) and/or clinical signs of instability.

As football is an inherently 'traumatic' sport in terms of mechanical joint loading and from contacts with the ball and other players, a diligent radiologist will report many 'positive' findings on MRI scans many of which may be noted but disregarded by the team physician when evaluating a player. Many such MRI findings represent normal adaptation responses to the demands of the sport or the stage of skeletal maturity of the player and are not necessarily pathological. Examples include transient marrow oedema in the pubic bones of an adolescent player (Fig. 1) or thickening of the medial collateral ligament of the knee in response to repetitive kicking and tackling actions. Other findings previously thought to be less significant radiologically such as 'bone bruises' following contact trauma are now taken more seriously and have been re-termed as micro-trabecular fractures in recognition of the underlying pathology (Fig. 2).

In my experience, MRI appearances 'over-grade' the severity of superficial ligament injuries when compared to a combination of clinical and ultrasound examination findings. Nevertheless MRI is essential to confirm the severity of deeper or internal joint ligament injuries such as knee cruciate ligament injury, particularly if the clinical signs are inconclusive (Fig. 3). MRI is the gold standard for imaging articular cartilage and meniscal cartilage injury, both of which may be acutely traumatic or chronically degenerative in origin in footballers or may occur in combination with ligament injury (Fig. 4). Bone marrow oedema on T2 or STIR sequences may indicate metabolic activity in an injured region such as the pars interarticularis of a lumbar vertebra or proximal shaft of a 5th metatarsal bone

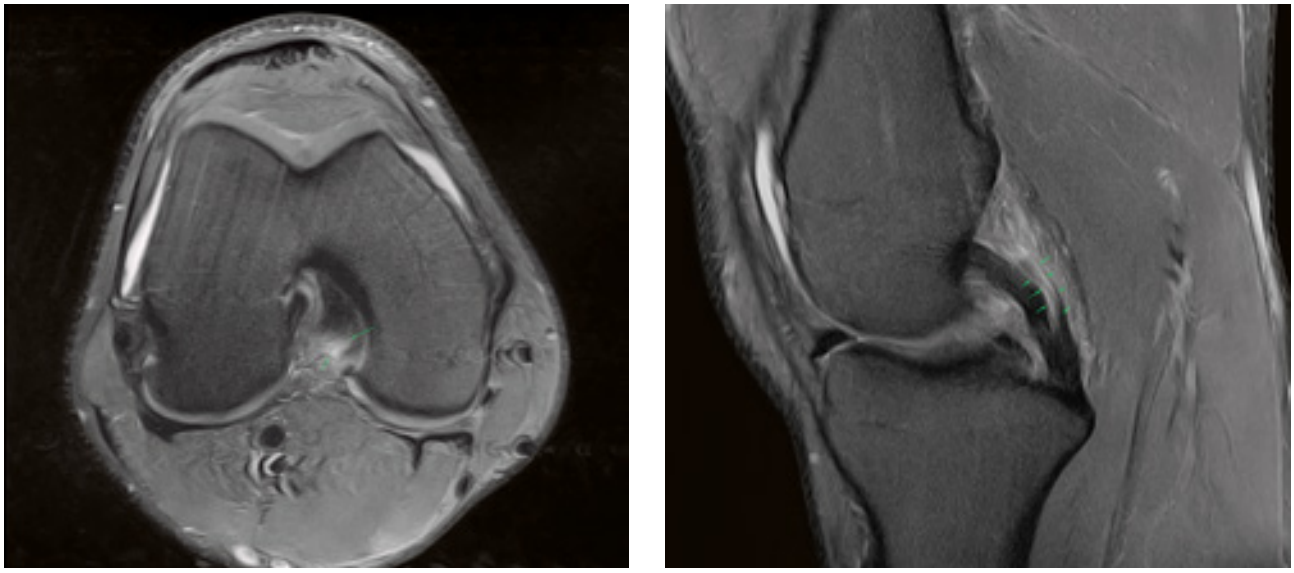

Figure 3: Axial & sagittal PD FS images of a footballer's right knee showing subtle oedema in the posteromedial bundle of the posterior cruciate ligament in keeping with a grade 1 sprain (green arrows).

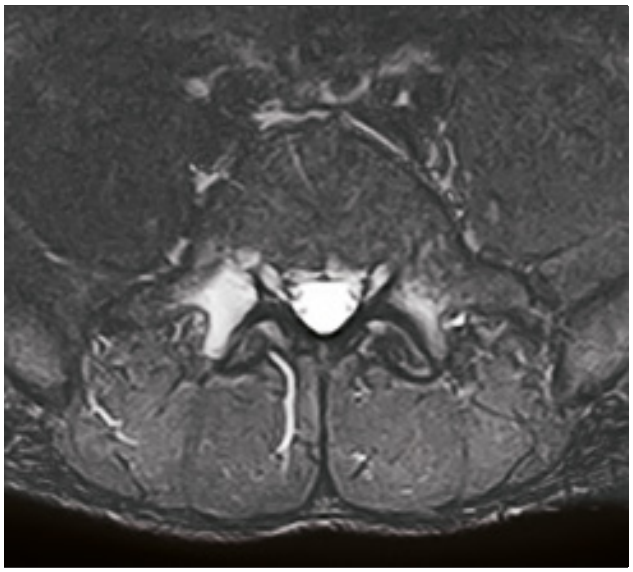

Figure 4: Axial STIR images of the 5th lumbar vertebra in a 20 year old footballer showing bilateral bone marrow oedema in the pars/pedicle region preceding eventual stress fracture formation.

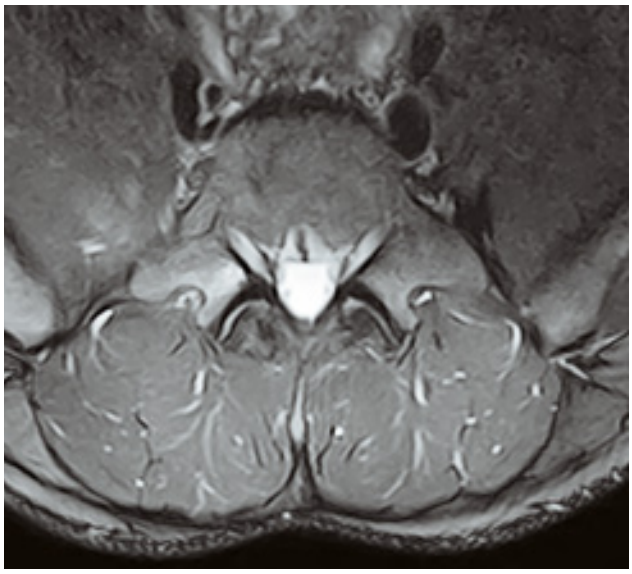

Figure 5: Localised residual oedema in the same player's right pars/pedicle region 8 months later (2 months after a return to full training).

in the foot (common stress fracture sites in footballers). Marrow oedema may persist long after functional recovery and bone loading capacity has returned so its presence must not be the sole arbiter of a return to training activities (Fig. 5).

CT scanning has some advantages over MRI when assessing certain bone and joint injuries and both may be needed in combination to fully evaluate a hip impingement or lumbar spine stress fracture. The increasing image resolution afforded via 3T MRI imaging, however, is of great value when safely screening or profiling young footballers for anatomical factors that might predispose them to typical football injuries, e.g. hip adductor muscle strains associated with pubic symphiseal or sacroiliac degeneration or CAM/pincer-type hip dysplasia (Fig. 6).

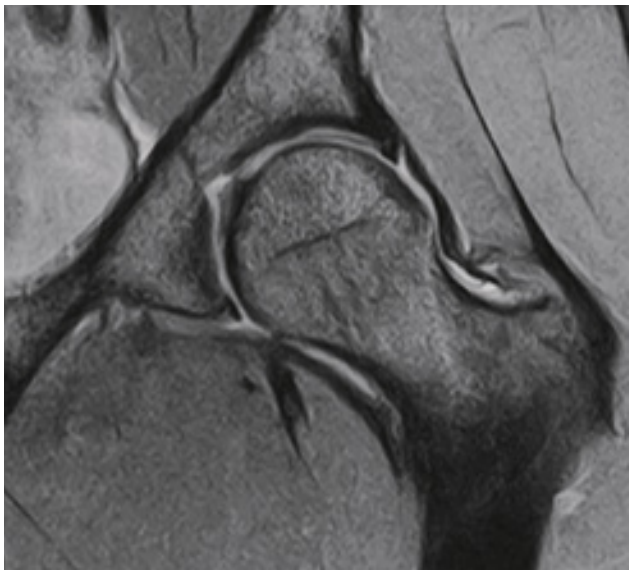

Figure 6: Coronal PD FS image of an 18 year old footballer's left hip showing CAM-type femoral head configuration with associated labral tear from repetitive impingement during kicking and running actions. Note the presence of pubic symphiseal degenerative changes, a common associated finding.

Muscle/tendon

MRI is most useful for differentiating between the 'MRI-positive' (i.e. oedema, haemorrhage +/- structural disruption) and the 'MRI-negative' (i.e. no oedema, haemorrhage or structural disruption). High resolution ultrasound scanning in combination with clinical history and examination is sufficient in most cases to confirm structural injury but can be less helpful in confirming a functional injury where subtle muscle oedema may be present. MRI can be 'over-sensitive' with regard to muscle oedema causing dilemmas for the treating practitioner when determining the pathological from the normal reactive increase in lymphatic and vascular fluid post-exercise.

Timing of MRI examination after clinical presentation is therefore important. 24 to 48 hours is generally accepted as sensible practice to reduce the risk of false negatives or positives by scanning too soon. The widely used Peetron's grading system to describe muscle oedema and structural disruption is being superseded by alternative classification systems bespoke to athlete muscle evaluation as they are deemed to be more specific or relevant to clinical decision making. These include classifications based on MRI appearances alone1 or those based on combining clinical presentations and examination findings with ultrasound and/or MRI appearances2 (Fig. 7 & 8).

Debate exists as to the validity of MRI in determining key factors for the player, therapist and coach such as prognosis and return to play decisions3,4 and there is no doubt that injured muscles can remain 'MRI-positive' for some time after functional recovery and return to play has been achieved6. Whilst the scientific research may not always be conclusive, experiential practice supports the use of MRI for accurate anatomical location and structural integrity assessment in key muscle injuries such as quadriceps, hamstrings and calf as the information gleaned can influence rehabilitation programmes in order to restore full performance whilst minimising re-injury risk. MRI may be the only way of identify deep groin/pelvic muscle injury in footballers that is beyond the depth of view of ultrasound scanning.

Footballers' tendon injuries are readily amenable to assessment by ultrasound in view of their relatively superficial location (patellar, Achilles, peroneal, tibialis posterior being those most often affected). The higher spatial resolution, the ability to assess dynamically

and with Doppler/Microvascular Imaging and Elastography/Tissue Characterisation make ultrasound the modality of choice in most cases but MRI can add value when assessing the musculotendinous junction particularly if structural injury is very subtle or when examining longer tendons that follow a convoluted course (e.g. peroneus longus/flexor hallucis longus). Newer MRI techniques (ultra-short TE sequencing) may begin to tilt the balance more in favour of MRI.

Screening/profiling

It is difficult in many clinical settings to justify the use of MRI as a screening tool if the word 'screening' is utilised correctly within context of the Wilson-Jungner criteria (see below).

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case finding should be a continuing process and a not "once for all" project.

In an elite football club setting, however, the relative definitions of terms such as 'important health problem' and 'economically balanced in relation to medical care as a whole' will be viewed differently and MRI becomes a more acceptable screening tool for certain conditions. In reality there is insufficient scientific evidence to meet some of the other criteria such as 'latent/asymptomatic early stages' and 'recognised treatment pathways' and the players expect their healthcare and performance optimisation to be managed on an individual basis albeit within a team 'population' setting. In view of that I prefer to avoid the term 'screening' and replace it with 'profiling' as that enables the individual player to be compared to himself over time (injury surveillance) or against a group which can be defined in many ways (age, ability, playing position, etc.). MRI can be a powerful addition to all the other aspects of health and performance profiling that medical & science professionals can undertake on footballers.

Examples of such profiling include body composition assessment, muscle length, cross-sectional area and volume, skeletal maturity that can be specific to areas relevant to football such as pelvis and knee joints as opposed to standardised wrist imaging for skeletal age estimation. Emerging techniques utilising 3T MRI can assist with profiling muscle fibre type and joint cartilage composition via non-invasive means which makes the assessment very acceptable to the athlete patient.

Since access to players for screening/profiling purposes can be difficult to obtain, having a dedicated MRI facility close to hand is essential. However, there is usually one opportunity to profile a player when he/she joins the club (although the nature of the transfer system can also make that very difficult at times).

The 'Signing/Transfer' medical

The common perception portrayed by the media is that footballers either 'pass' or 'fail' their transfer medicals when joining a new club. As there are no legislative or industry-defined criteria for fitness to play professionally this is not strictly true. Each scenario will be different depending on the context of the transfer and this might be influenced by the duration of the proposed contract, the size of the transfer fee, the terms and conditions of the contract and financial aspects such as salaries and agent's fees. The process is more one of risk assessment and an opportunity to gather baseline information in order to assist with the player's subsequent medical care should he/she join the club. Whilst a transfer medical can be likened to a pre-employment medical where the initial duty of care is to the employer, a duty of care is also assumed towards the player whether

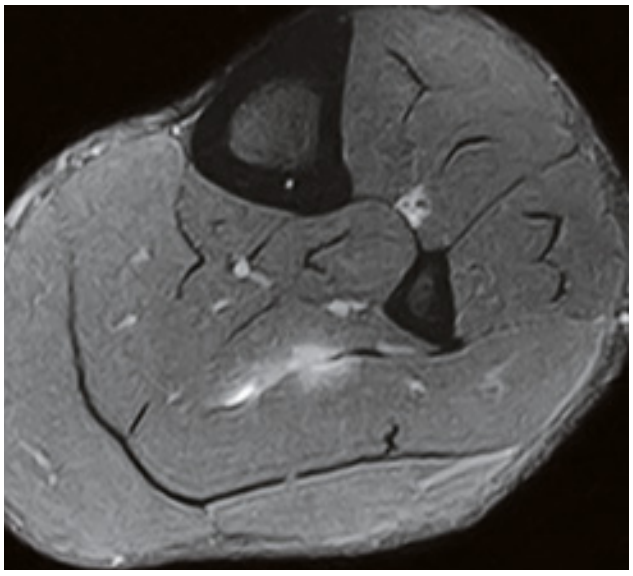

Figure 7: Axial PD FS image of a footballer's left calf muscle showing subtle oedema in the deep lateral soleus musculotendinous junction consistent with minor functional or very low grade structural injury.

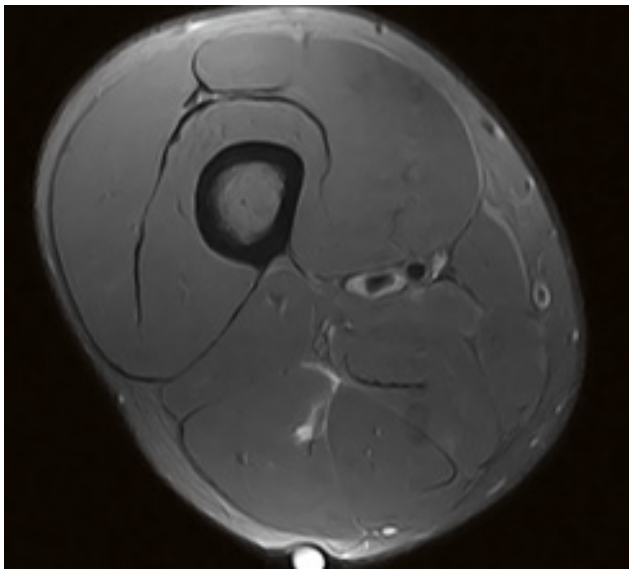

Figure 8: Axial PD FS image of a footballer's right thigh showing a localised structural defect at the biceps femoris musculotendinous junction with high signal extending from that into the myofascial space consistent with a moderate partial muscle tear (Munich Classification Type 3B).

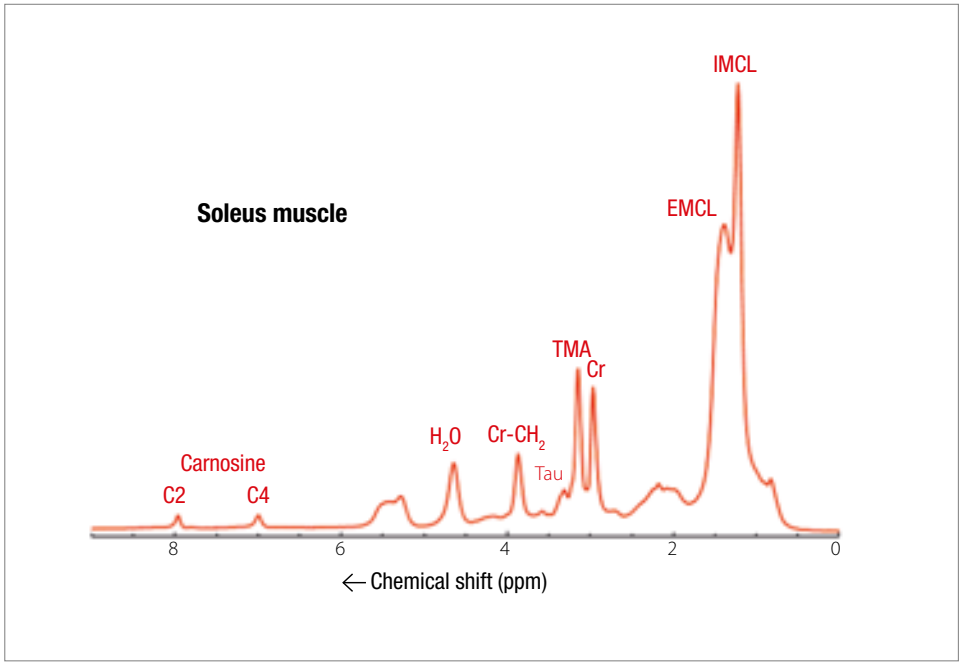

Figure 9: Spectroscopy of soleus muscle to assess carnosine content as an indicator of type 2 'fast-twitch' muscle fibre proportion.

he eventually signs or not, particularly if adverse findings are detected. MRI scanning can therefore be very informative but also fraught with ethical and medicolegal issues in such circumstances.

One of the major limiting factors in transfer medicals is time available, particularly if it takes place near the end of the transfer window periods. MRI scanning is usually the most time- consuming aspect of the medical assessment, even if limited sequence protocols are employed, and it might be impossible to include MRI if a transfer takes place in the final hours of 'deadline day'. Wherever possible it is our policy to include a limited sequence protocol examining lumbar spine, pelvis, hips, knees and ankles with additional sequences if clinically indicated from history and physical/functional examination. The scanning time needed is around 2.5 hours plus any transport time if this has to be undertaken at a remote facility. It's a long time for a player to be on the scanner table so maximising comfort and minimising sequence time is essential for full compliance and a positive 'first experience' for the player at his/her intended new club.

Although there is no consensus amongst football medics regarding the value of transfer medical MRI and many medicals take place without them being performed, it seems logical that the more information one is aware of when investing in a high value player the better, especially with regard to the detection of asymptomatic or subclinical pathology. Evolving articular cartilage lesions in joints or painless degenerative tendinosis might not cause a problem but could also be performance-limiting and potentially career-threatening; knowing about their presence in advance can help by modification of training loads and initiation of preventative programmes as part of asset management. MRI provides a baseline checkpoint which can be referred back to for comparison if needed.

As decisions, risk assessments and recommendations are usually required immediately after completion of the medical examinations it's vital to have experienced radiologists available 24/7 to report and discuss within clinical and functional context. In high value transfers it is not unusual to undertake 'double reporting' to seek a range of unbiased opinion.

'Performance' imaging

In addition to standard anatomical MRI, post-processing applications can visualise structures in a more impactful manner (e.g. fat and lean mass) and quantify muscle tissue dimensions and volume. This can be very important for monitoring results of conditioning or rehabilitation programmes when comparing the player to him/herself or to a population of players who have been profiled in a similar manner.

MRI spectroscopy can be utilised to measure amounts of substances key to muscle function or fibre type composition, e.g. carnosine content is closely related to the proportion of fast-twitch fibres a player has within the muscle5. This can have implications for his/her genetically-determined performance potential, prescription of training programmes and recovery strategies post exercise (Fig. 9).

Compositional assessment of joint cartilage7 is an exciting new development for football medicine as it has the capacity to detect microstructural and biochemical changes within the articular cartilage before eventual structural defects become apparent on standard MRI. Whilst many players are able to play professionally with established articular cartilage defects this pathology is one of the major career-limiting factors for a footballer if hip, knee or ankle are affected. Even if able to play without recurring joint pain, swelling or mechanical dysfunction, secondary injury or performance impairment is likely due to associated muscle inhibition or protective hypertonicity. The ability to detect pre-symptomatic changes in the cartilage by quantitative T2 mapping may facilitate early implementation of preventative strategies thereby prolonging athletic performance and the long-term health of the joint beyond the playing career.

1.5T v 3T

Although scanning with a 3T rather than a 1.5T scanner will not alter the subsequent clinical management in the majority of cases of typical football injury[8], 3T does offer advantages in terms of reduced scanning time (and hence patient comfort and acceptability). If time is no issue, better image quality is possible particularly for smaller joints such as the foot or wrist where subtle ligament or joint injury might otherwise go undetected. The radiographer and radiologist

will need to amend their 1.5T techniques and some time may be required to fine-tune a 3T scanner to the area under examination. The effort will be worthwhile leading as it leads to beautiful images. Findings that previously were impossible to detect need to be interpreted carefully in conjunction with the treating sports physician. Another advantage of 3T MRI in the sports medicine setting is that emerging technologies such as those described above for performance profiling are more readily applicable in higher field strengths.

Summary

As the physical demands of professional football and the financial investments in the industry continue to increase year on year, the pressure on club medical & science teams to maintain their players in top condition also increases. Some injuries are inevitable and the aim then is to return the player to the pitch at the required performance level with minimised risk of re-injury in the shortest possible time. MRI has a role to play in that overall process and it will continue to evolve as technologies develop and practitioners become familiar and confident in applying them within this unique area of sports medicine. //

Dr Steve McNally
Head of Football Medicine & Science Manchester United, United Kingdom.

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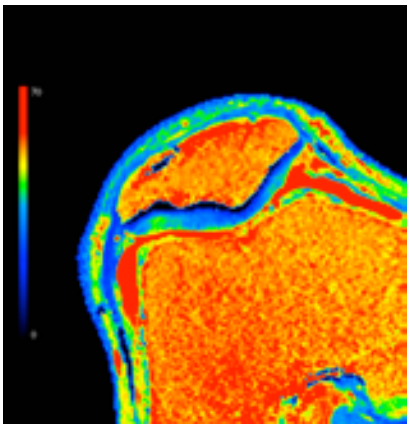
M-Power - Zen Edition Features

With the introduction of M-Power version 4.0 (Zen Edition), a rich set of new sequences, functionalities and options have become available for the Vantage Galan™ 3T, Vantage Titan™ 3T*, Vantage Titan™ 1.5T and the Vantage Elan™.

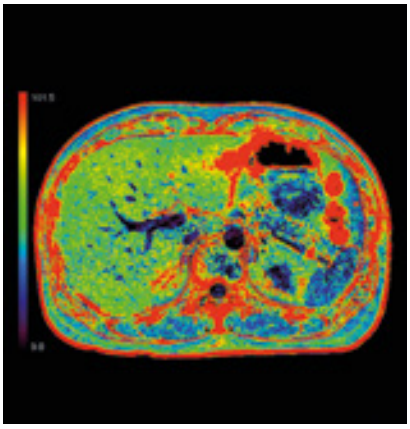
T2 and T2* Mapping Using mEcho FSE and FE

Using 2D Fast Spin Echo sequences allows for T2-map calculation for i.e. cartilage mapping in MSK. Maps of other anatomical areas are available as well.

2D Gradient Echo sequences are used to generate T2* and R2* maps to analyze Iron quantification in the liver.



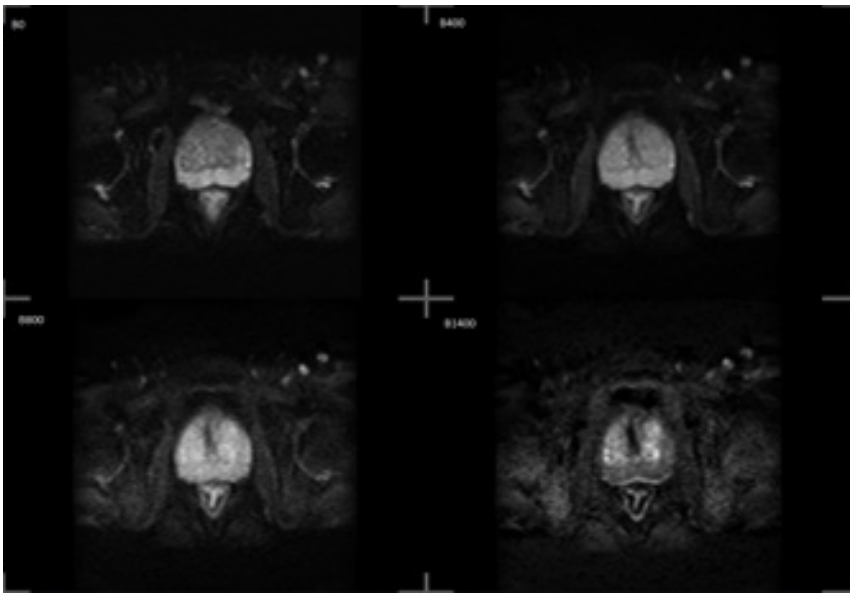
Fusion with colored T2 map image



R2 Calculation Result*

Multi-B - Using up to 15 B-Values in One Sequence

With the Multi-b Diffusion sequence up to 15 b-values, ranging from 1 - 10000, may be prescribed in one sequence.
Using post-processing other b-values may be calculated, (cDWI).

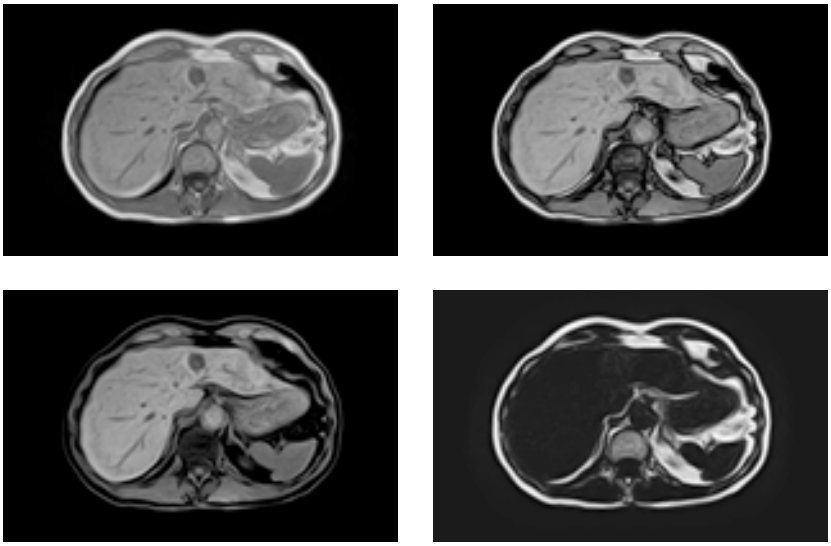


* *Available for the Vantage Titan 3T with Saturn Gradient*

DIXON (Water Fat Separation)

With the Dixon technique four image contrasts are generated: Water only, Fat only, In-Phase and Out-Of Phase images.

These images can be used, for example, to perform Fat Quantification (using Olea software).
Furthermore, excellent high resolution Fat suppressed images, without the need for an additional RF pulse (increased SAR),can be achieved.

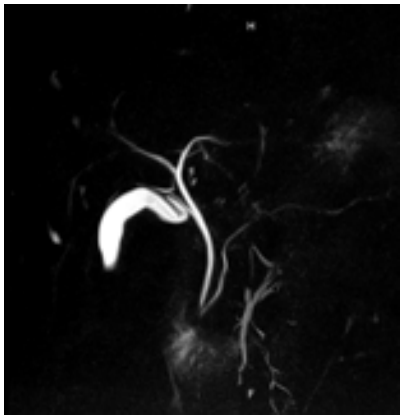


Abdomen Free Breathing

Abdominal scanning without breath hold commands.

Using the Free Breathing Technique in abdominal imaging reduces the stress and burden of breath hold scanning for the patient, yielding images with excellent image quality.

Patient set up does not require additional gating devices and bellows.

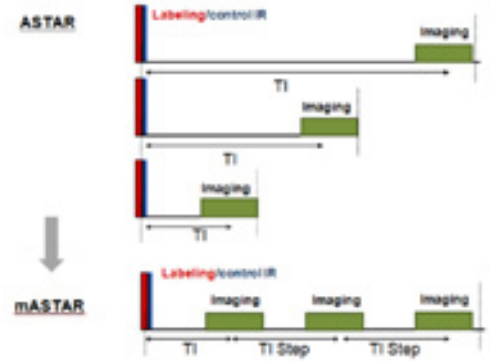


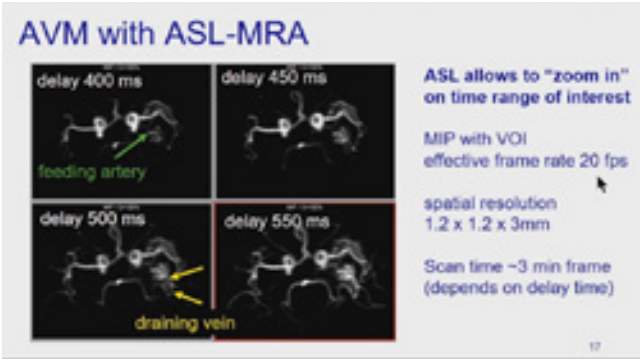
MRCP: Free breathing
Scan time: 2:55

mASTAR

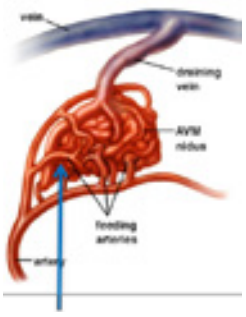
mASTAR is an Arterial Spin Labeling technique using the ASTAR method.
It can be used to obtain 4D non-contrast MR Angiography images in order to visualize i.e. Arterio Venous Malformations (AVM).

mASTAR reduces scan time vs. normal ASTAR.
It can acquire 7 time frames in one sequence in 5 min. 10 sec.





Courtesy of VU University Medical Center Amsterdam



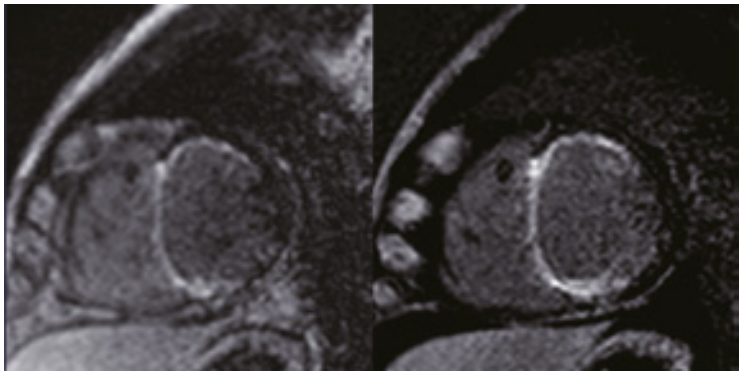
Stereotactic Radiation Surgery Target

M-Power - Zen Edition Cardiac Features

PSIR (Phase Sensitive Inversion Recovery)

PSIR in the heart provides improved contrast in late-enhanced imaging by using a more robust nulling of healthy myocardial Signal without the need for an inversion time (TI) calibration scan.

By eliminating the need for calibration, cardiac examinations can be completed with fewer breath holds and greater patient comfort.



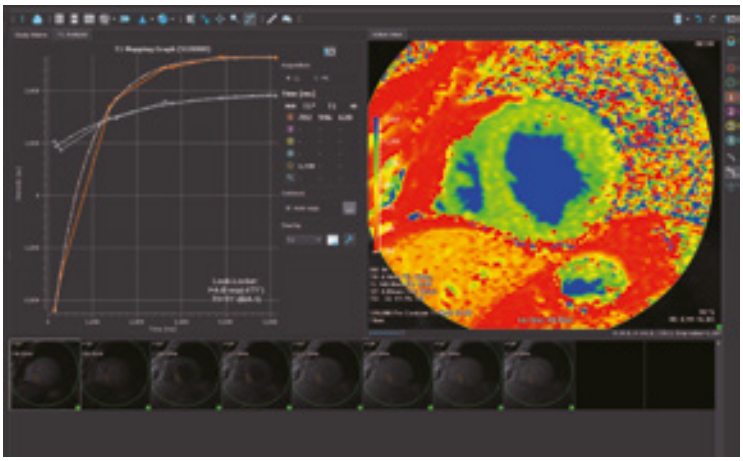
Delayed Enhancement *PSIR*

Courtesy of Instituto do Coração

MOLLI (MOdified Look-Locker Inversion recovery)

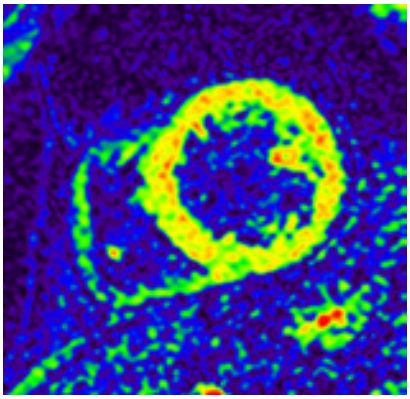
MOLLI sequence for Cardiac Imaging. Expand your cardiac toolset with T1 mapping, allowing you to acquire a much more quantitative characterization of myocardial tissue.

Toshiba Medical's T1 mapping utilizes a MOLLI sequence, enabling the acquisition of a full T1 map within a single breath hold.



Post-processing on Medis software

Courtesy of Instituto do Coração

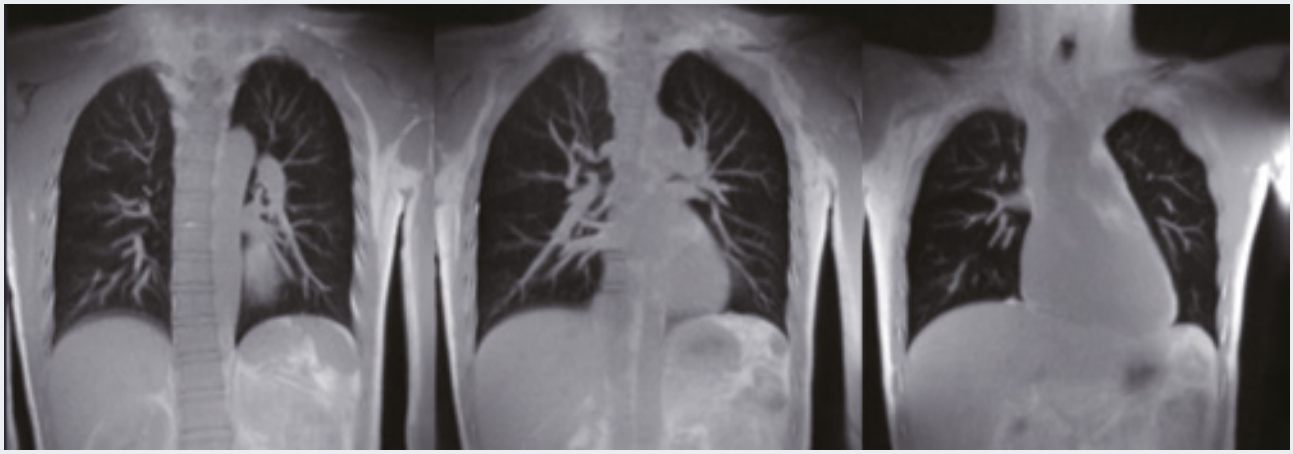


Colored Cardiac T1-map

M-Power - Zen Edition Optional Features

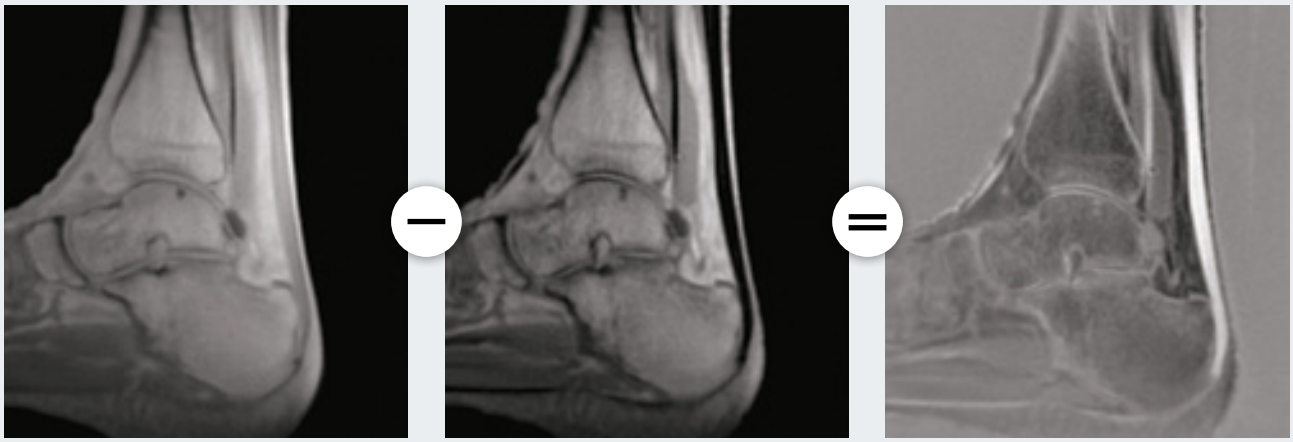
UTE (Ultrashort Echo Time) Lung and MSK Imaging Example

UTE acquires data in a radial pattern from the center of the k-space, immediately after the RF excitation pulse is applied. It enables the depiction of tissues with very short T2* values, such as the lung.



UTE, Lung tissue imaging example

Acquisition of tissue with short and longer TE → subtraction → UTE image.



Ultrashort TE

longer TE

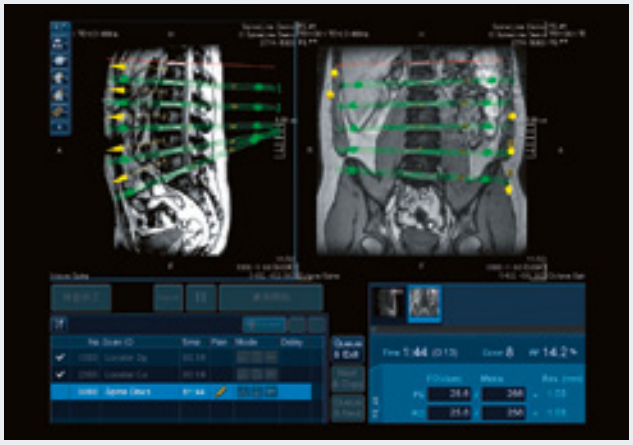
Subtracted UTE image

EasyTech

Improve workflow with a suite of auto alignment tools to guide the operator through the process from beginning to end. EasyTech offers automatic slice alignment and positioning for cardiac, neuro and spine exams.

SpineLine

With its auto-locator functionality, SpineLine allows you to plan spine studies quickly and easily. Sagittal and coronal locators allow you to set double-oblique slices, enhancing the reproducibility of follow-up exams.



SpineLine

NeuroLine+

Achieve outstanding scan consistency for all your brain exams with NeuroLine+. The function's intelligent alignment algorithm allows you to automatically set up according to AC-PC and OM line.

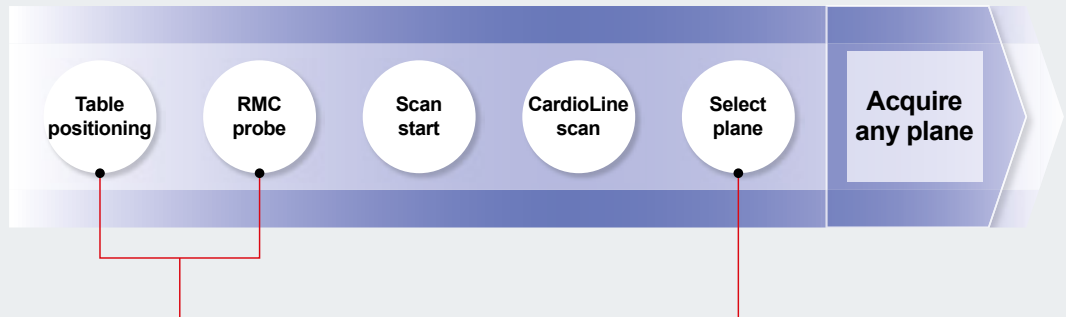
NeuroLine+

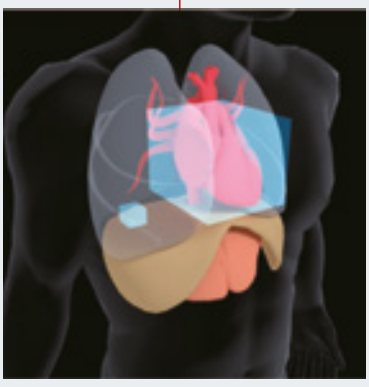
SUREVOI™ Cardiac

Automatic detection of heart and liver with a non-rigid model allows for full workow automation from table positioning to the Real-time Motion Correction (RMC), probe placement and fully automated cardiac planning.

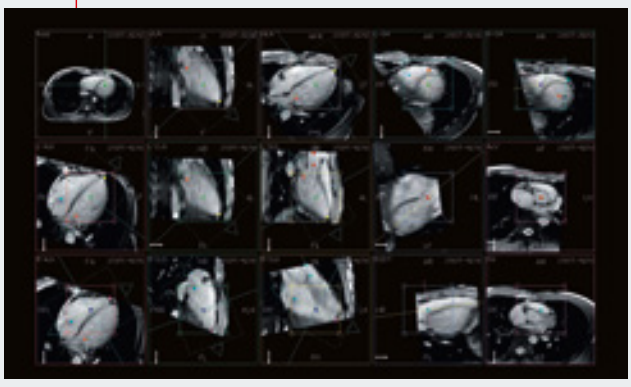
CardioLine+

CardioLine+ automatically identies the 14 standard cardiac planes including right and left ventricle, as well as the four cardiac valves in a single breath-hold scan.





SUREVOI Cardiac



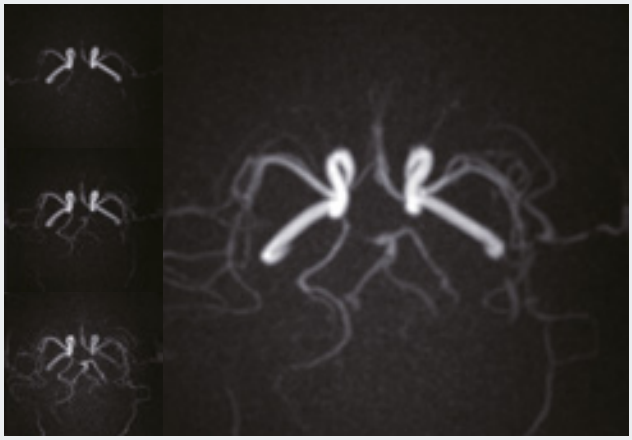
CardioLine+

Pianissimo Zen

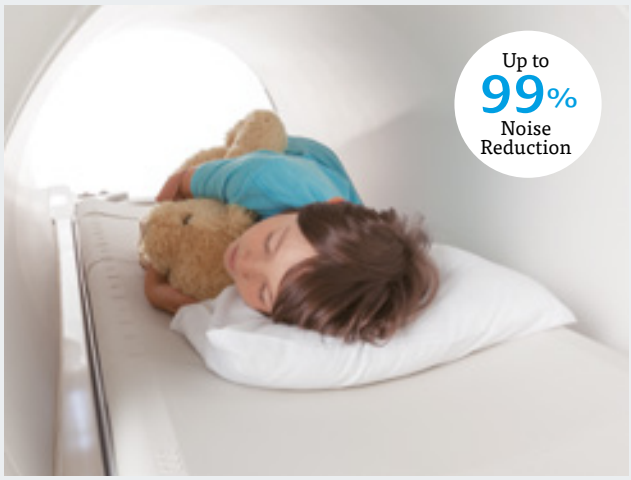
MR acoustic noise is one of the major complaints of patients and medical sta. Toshiba Medical's patented Pianissimo acoustic shielding technology signicantly reduces the noise in and around the MRI environment for every sequence, every scan and every patient.

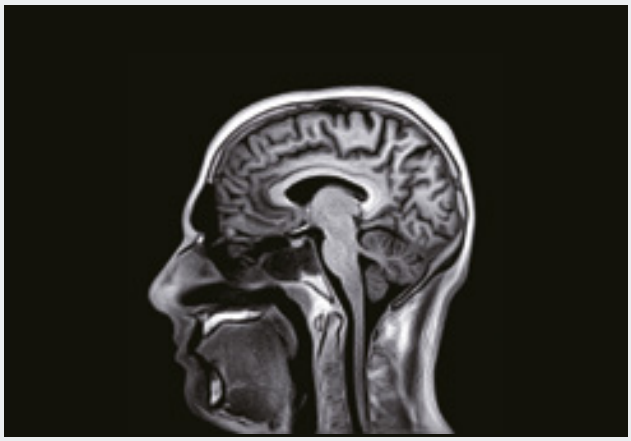
Pianissimo Zen quiet sequences further reduce noise to just above ambient noise level, making exams even more comfortable and easier to complete.

[1] *mUTE : minimized acoustic noise utilizing UTE*



mUTE[1] / mUTE 4D-MRA





mUTE[1] 3D T1

MR Theater 1*

Zen Edition offers an immersive in-bore MR Theater option. As the images displayed appear to be much farther away than the actual bore, the MR Theater provides a uniquely comfortable experience, encouraging patients to relax and stay still during the MR exam.

** Optional for Vantage Galan 3T and Vantage Titan 1.5T*

Some features presented in this article may not be commercially available on all systems shown or may require the purchase of additional options. Please contact your local Toshiba Medical representative for details.

TOSHIBA
MEDICAL

Together, we complete the image.

Made For life

Made for Partnerships.
Made for Patients.
Made for You.

At Toshiba Medical we partner with our customers to truly understand their needs in imaging and beyond.

We develop a full range of imaging solutions, including CT, X-Ray, Ultrasound and MR that address time pressures, workflow constraints, patient comfort and imaging precision to deliver true efficiency coupled with best in class tools for diagnosis.

Together, we work on an education plan and develop service solutions that meet your every need.

Our goal is to work hand in hand with our partners to deliver optimum health opportunities for patients through uncompromised performance, comfort and imaging accuracy. Together, we complete the image.

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Canon
CANON GROUP

Clinical usefulness of 3T UTE imaging on MSK

Creu Blanca Group, in Barcelona and Zaragoza (Spain), is a family business with 67 years of experience in the healthcare sector. With currently over 350 health professionals collaborating with them and a staff of 200 people Creu Blanca attends more than 300,000 customers annually, and makes an average of 600,000 annual medical acts.

Dr. Alomar currently serves as Head of the Radiology Department and R&D at Medical Centers Creu Blanca. He holds a Doctor of Medicine degree with specialization in Radiology from Hospital de la Santa Creu i Sant Pau in Barcelona, Spain.

With over 27 years of experience in Diagnostic Imaging, particularly computer tomography and magnetic resonance, Dr. Alomar has contributed to a number of studies and papers in local and international scientic publications, to include AJR and RSNA. He has focused his clinical and research interests in orthopedic, angiography, cardiology, body imaging, women's and men's health.

Dr. Alomar: "I would like to state that the Toshiba Medical's magnetic resonance imaging (MRI) scanner contains a new package of sequence including a 3D FFE sequence which enables me to get high resolution isotropic images (e.g. 1 mm) with ultra-short TEs (e.g. 0.09 ms).

This sequence is very robust, reproducible, stable and non-prone to artifacts; features which make it instrumental in clinical routine. I am very excited with this sequence because it will allow us to assess the structure of tissues with extremely short T2* value (e.g. tendons, ligaments, osteochondral joints, fibrosis) which cannot be evaluated with conventional sequences.

In addition to musculoskeletal studies, I foresee that this sequence will be also relevant in other clinical applications such as depicting lungs without radiation exposure".

Case Studies

Our experiences with the Toshiba Medical MRI scanner is best to describe in some clincal cases. See the the next pages.

Mrs Elena Ferre, Chief of Radiographers and Dr. Alomar, Head of Radiology Department and R&D Medical Centers of Creu Blanca

About Group Creu Blanca

Creu Blanca is a family business with 67 years of experience in the healthcare sector. Currently we have over 350 health professionals who actively collaborate with us and a sta of 200 people. The management of the group is completely centralized, which facilitates and streamlines the management of appointments, billing, and nally, the Customer Relations. We attend more than 300,000 Customers annually, and make an average of 600,000 annual medical acts. We are present in Barcelona and Zaragoza.

In Barcelona:

- *2 Medical Centers (Creu Blanca Pelayo and Creu Blanca Tarradellas)*
- *1 Polyclinic (Diagnosis Médica)*
- *1 Hospital: Clínica Creu Blanca*

In Zaragoza:

- *1 Polyclinic (Policlínica Sagasta)*
- *1 Diagnostic Center (Paracelso Diagnóstico Médico)*

We have a large variety of equipment that allows us to perform from the simplest to the most complex explorations:

- *13 MRI (3 of them of 3 Tesla)*
- *3 CT Scanners*
- *30 Ultrasound systems*
- *30 XR systems*
- *2 SPEC systems*
- *1 Interventional XR Room*
- *3 Digital Mammography systems with Tomosynthesis*
- *150 Medical Oces*
- *Emergency Service*
- *4 Surgery rooms and 25 boxes for Outpatient*
- *50 Hospital rooms.*
- *1 PET - CT.*

CASE STUDIES

Case 1

Patient history

16 year-old male. Pain, swelling and instability after knee trauma.

Imaging Findings

T2 FSE sequences show bone edema within the external femoral condyle, with a fracture line in the subcortical trabecular bone without delimiting discontinuity of the cortical bone or articular cartilage.

UTE (ultra-short TE) sequences allow for the visualization of low signal in the cartilage, as well as the cortical area of the bone previously identied on the T2 sequences. This area is divided in 2 layers, a superficial one of high signal in the UTE which corresponds to the osteochondral area or tidemark, and a deeper cortical bone area. At the level of the subchondral fracture, discontinuity of the double line in the cortical bone was not identified, which signifies its integrity.

The T2 sequences show thickening of the ACL fibers with signal abnormalities in their proximal area. The UTE sequences also display signal abnormalities.

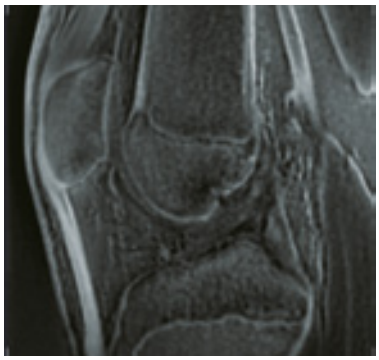
Discussion

UTE is a new sequencing option, characterized by the ability to acquire 3D gradient echo images with echo times (TE's) of less than one millisecond. This allows us to evaluate structures with very short echo times such as connective tissue, fibrosis, and osteochondral unions. Previously these structures could not be evaluated with MR due to the low signal that results from their very short TE's.

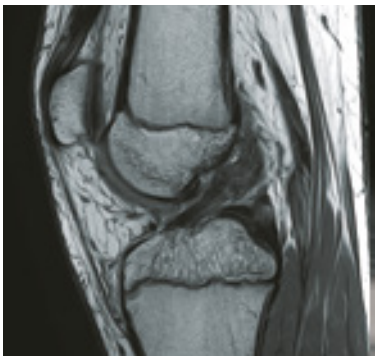
The process is simple: two UTE sequences are acquired with respective TE's of 2 ms and 0.09 ms, an isotropic pixel resolution of 0.4 x 0.4 (matrix of 412 x 412), and a scan time of approximately 4 minutes per sequence. This is followed by a subtraction between the two dierent TE's. The resulting images are used to evaluate connective tissues.

Conclusion

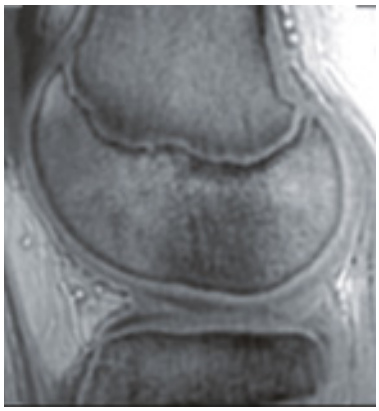
Thanks to UTE sequencing, we are now able to evaluate a series of anatomical structures which have been previously overlooked due to their short relaxation times and low hydrogen content. Most important amongst these structures are connective tissues and their derivatives (such as tendons meniscus, ligaments, and osteochondral structures) and their many pathologies. In our case, UTE permitted us to rule out osteochondral pathology.



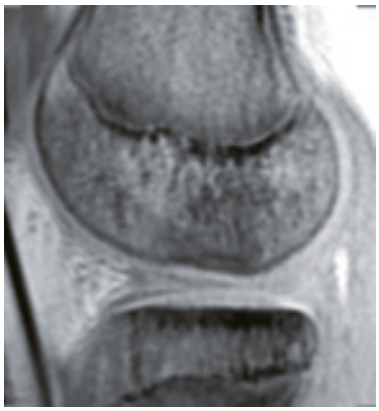
Subtracted UTE. Signal abnormality on ACL fibers.



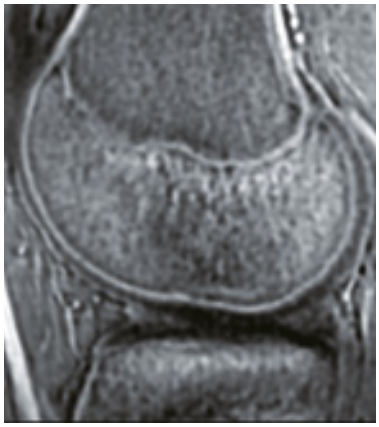
T2 Sequence. Full rupture of the proximal ACL.



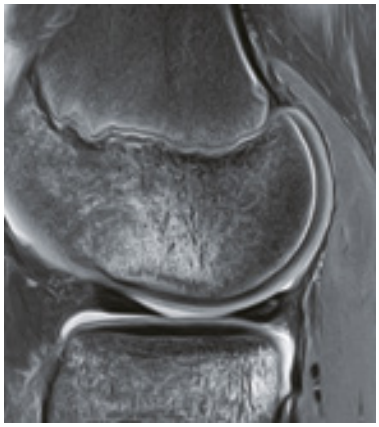
UTE Sequence. TE=0.09 ms.



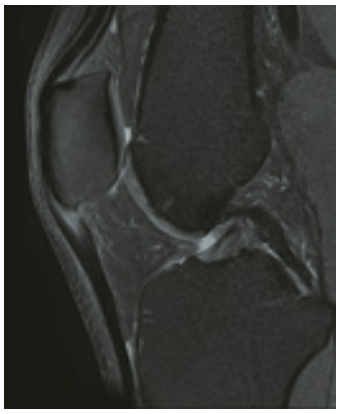
UTE Sequence. TE=2 ms.



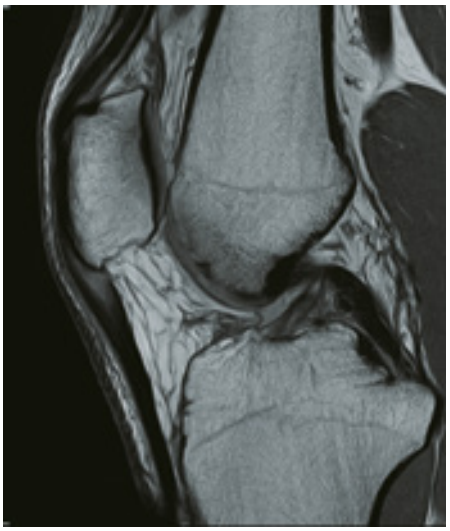
Subtraction Image obtained from both TEs (2ms;0.09ms). Note the double line in the cortical bone. The deeper line is black, and the superficial (adjacent to the cartilage) white, on both the contusion area as well as on the rest of the articular surface.



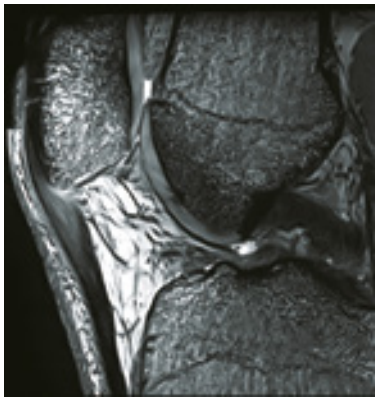
T2 FSE. Bone edema and fracture of subchondral trabecular bone.



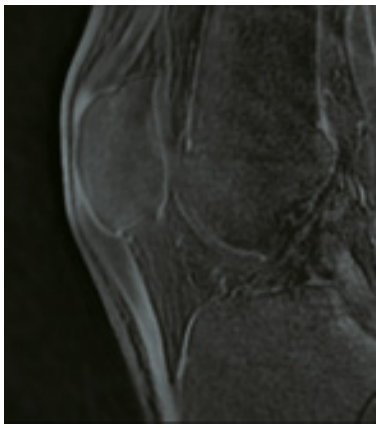
T2 FSE FS. Area of focal edema at the proximal insertion of the patellar tendon.



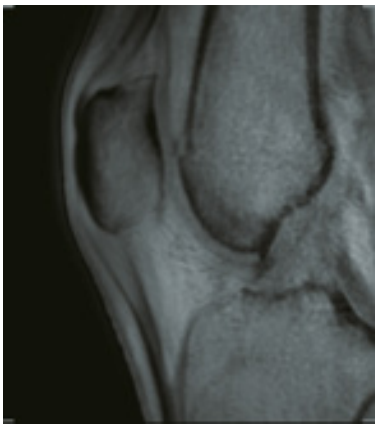
T2 FSE. Area of focal edema at the proximal insertion of the patellar tendon.



FE3D shows chondral irregularities with subchondral lesion and areas of chondral ossifications.



Subtracted UTE. Thickened patellar tendon at the proximal insertion with inside areas of low signal intensities. Compared with the classic sequences T2 FSE and FE3D, the size of the tendinous lesion is better appreciated in the UTE sequences.



UTE. TE=2 ms.

Case 2

Patient history

33 year-old male athlete. Presents with infrapatellar pain after exercise.

Imaging Findings

T2 FSE and 3D gradient sequences display thickening with abnormal signal and edema of the patellar tendon on the patellar insertion, central fibers, without fibrillary discontinuity and with adjacent normal Hoffa fat. The UTE sequence demonstrates thickening with signal abnormality of the central patellar fibers along their insertion, while both the superficial and deeper tendon fibers show normal signal intensities.

An area of Grade 1 Chondropathia in the trochlear region, with areas of fibrocartilage, subchondral lesions and some areas of chondral delamination, is seen on both the T2 FSE and 3D gradient sequences.

In the UTE sequences, we did not observe the double line (black/white) in the cortical osseous trochlear region, as opposed to the patellar zone, where the line is clearly delimited, a sign of integrity of the osteochondral or tidemark zone.

Discussion

With UTE sequences, we can evaluate different grades of intratendinous edema. While acute tendinopathy can be easily be seen on regular T2 FSE and 3D gradient sequences, as the pathology resolves, so does the edema, making it difficult to differentiate the grades of chronic tendinitis. Thanks to the new UTE technique, we can evaluate high signal regions, particularly in these areas where basic sequences could not routinely do so.

Conclusion

It is probable that in the future, by utilizing this new sequencing technique, we will be able to better evaluate different grades of chronic tendinopathy and better understand the process of degenerative tendinopathy, as well as quantify the results of various treatments for these conditions.

Case 3

Patient history

75 year-old male. History of Achilles tendon rupture and post-surgical changes. 6 month follow-up showed good clinical evolution.

Imaging Findings

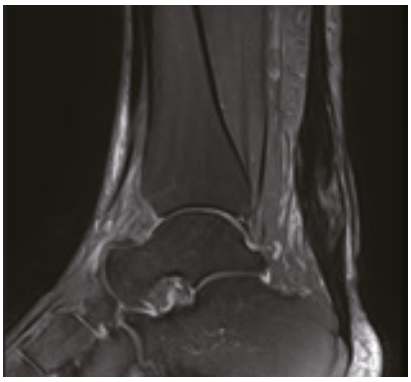
Considerable thickening with signal abnormalities of the Achilles tendon on the T1 and T2 FSE sequences, as well as continuity of the tendon and some areas of internal myxoid degeneration, are seen. The UTE sequence identified the most extensive signal abnormality in the Achilles tendon in comparison to T2 and T1 sequences, corresponding to areas of tendinopathy and regeneration of subacute phases and delimiting the regenerative zones of healthy tendon. In the UTE sequences, we cannot identify the areas of myxoid degeneration or the areas of fibrillary discontinuity but we can see more clearly the surgical metallic artifacts and evaluate the areas that surround them.

Discussion

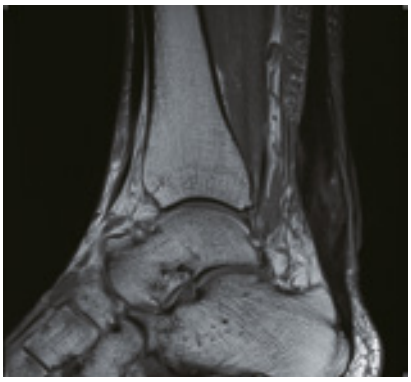
By using UTE sequences, we can evaluate the different stages of chronic tendinopathy after surgery, allowing better delineation between healthy tendon and areas of regeneration, as well as the surgical zones, but we cannot differentiate areas of fibrillary discontinuity and myxoid degeneration from areas of tendinosis and regeneration.

Conclusion

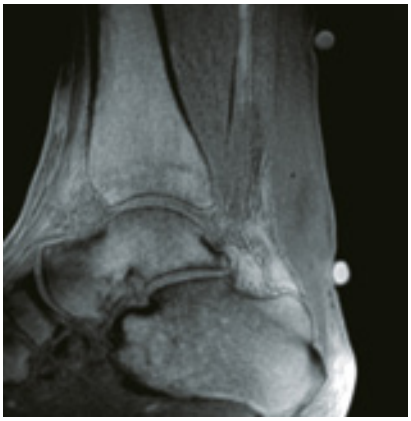
UTE permits a better evaluation of regenerative or discontinuous tendons and post-surgical tendons, as well as the evolution of final stages of chronic tendinopathies. However, UTE should not be used to assess the degree of fibrillary discontinuity in acute lesions, the degree of retraction in tendons, or areas of myxoid degeneration.



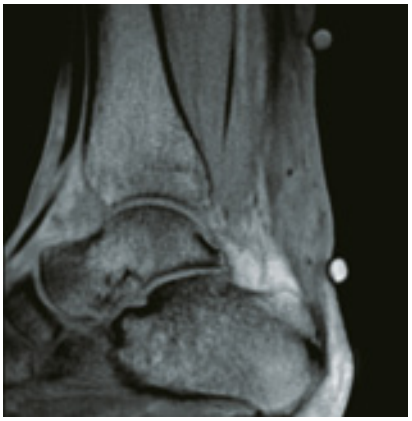
T2 FSE with Fat Saturation.
Large chronic tendinosis area of low signal on T2 with an area of myxoid degeneration and fibrillary discontinuity. This area is not identied on the UTE images.



T1 FSE. Similar findings as in the T2 sequence.



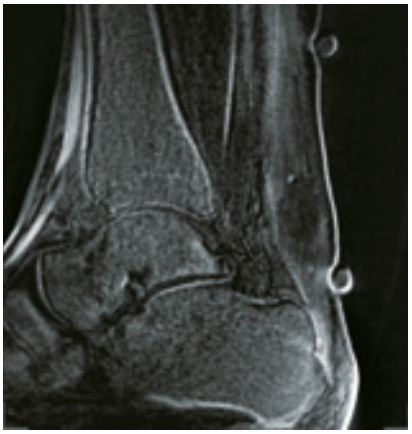
UTE Sequence. TE=0.09 ms.



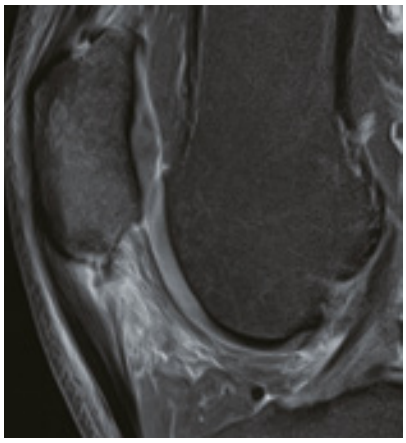
UTE Sequence. TE=2 ms. Post-surgical artifacts clearly depicted.

" This 3D FFE sequence will allow us to assess the structure of tissues with extremely short T2 value."*

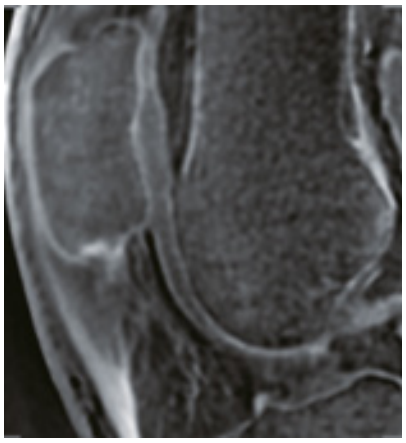
Dr. Alomar



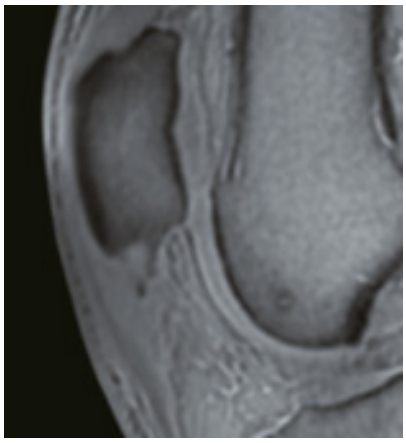
UTE Subtraction.
Diffuse alteration in the Achilles tendon signal in the operative zone delimited at its ends with healthy tendons and interior fascicles.



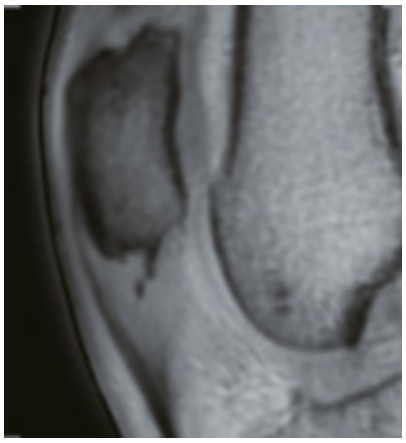
T2 FSE with Fat Saturation.
Thickening with signal abnormality at the proximal patellar insertion. Discontinuity of the deep fibers, small foci of edema in the patella and Hoffa fat. The size of the tendinous edema is smaller here than in the UTE subtracted sequences



Subtracted UTE sequence.
Thickening of the patellar tendon at the proximal insertion with bad delineation of the deep fibers and affecting the Hoffa fat.



UTE Sequence. TE=0.09 ms.
Depiction of proximal insertion calcifications.



UTE Sequence. TE=2 ms.
Tendon calcifications are better depicted proximally

Case 4

Patient history

28 year-old male basketball player. Presents with increasing pain over the last two years in the inferior pole of the patella.

Imaging Findings

Sub-acute tendinopathy with areas of chronic tendinopathy at the level of the proximal insertion of the patellar tendon, with focal tendon edema, osseous edema in the patella, and fibrillary discontinuity of deep fibers and edema in the Hoffa fat are all clearly observed in the FSE T2 sequences. UTE sequences show better depiction of the tendinous calcifications and the greater extension of the tendinopathy.

Discussion

UTE sequences can be used to better determine the grade and extent of tendinous degeneration in the context of acute chronic tendinopathy in addition to intratendinous calcifications. At the same time, it is less sensitive in the assessment of fibrillary discontinuity in the cystic cavities, intra-tendinous myxoid degenerations, osseous edemas, and edemas in Hoffa fat.

Conclusion

In the future, use of UTE as a complimentary technique may become essential for assessing the degree and extension of acute, subacute and chronic tendinopathy, as well as for follow-up. However, it will not replace routine FSE T2 and 3D gradient sequences as they provide better visualization of fibrillary discontinuity and involvement of adjacent structures. //

DWI of the Prostate

François Cornud, MD / Thibaut Pierre / Paul Legmann, MD

Should we use quantitative metrics to better characterize focal lesions originating in the peripheral zone?

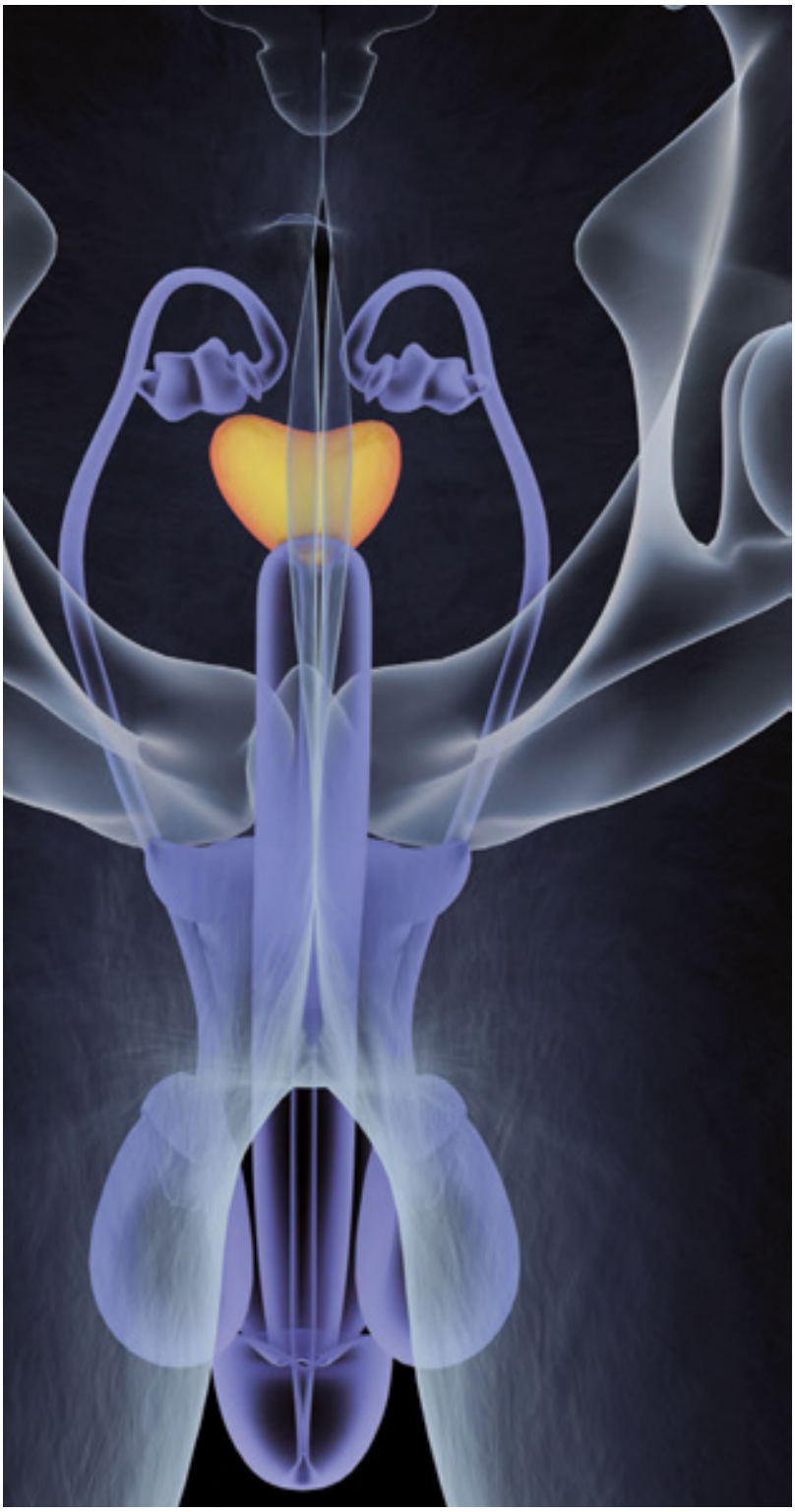
DW-MRI of the prostate plays a central role in prostate MRI. It is considered as the dominant sequence in the peripheral zone (PZ)[1]. If combined with T2W images, it also improves the accuracy of MRI for the detection of transitional zone cancer (TZ Ca)[2,3].

To characterize a focal lesion visible on MRI, a 1 to 5 scale is used. A score of 4 or 5 results in a cancer detection rate of 70-100%[4], whereas a score of 1 or 2 has been found to generally represent benign tissue[4]. As a result, it is now recommended to routinely perform MR-targeted biopsy of score 4 or 5 lesions, while considering deferment of biopsy for low-probability lesions.

However, management of score 3 lesions remains unclear, because the visual assessment of the combination of the Signal Intensity (SI) on the apparent diffusion coefficient (ADC) map and source DW images (dark on the ADC map and bright on source DW images), which characterizes score 4 and 5 lesions, is not straightforward in score 3 lesions. Visual assessment of these lesions is labelled "mildly hypointense" on the ADC map and "iso or mildly hyperintense" on the DW source images at a b-value >1000 s/mm² (i.e 1500 or 2000 in most studies), which entails a part of subjectivity.

Currently, targeted biopsies of score 3 lesions are recommended, but the cancer detection rate is low, approximately 20%[4], which contributes largely to the low specificity of the Likert or PIRADS scoring systems, lower than 50%[5]. The value of DW-MRI metrics deserved thus to be explored to improve the specificity of DW-MRI to characterize focal prostatic lesions, especially score 3 lesions. The most often used parameter has been the absolute value of the ADC, but several studies have proposed other parameters derived from the ADC map to improve the diagnostic and prognostic values of ADC metrics.

This review aims to show the different quantitative parameters available to evaluate the performance of quantitative MRI with a special focus on score 3 lesions.



Quantitative DWI and detection of PZ PCA

The ADC map

Numerous publications have established that the mean ADC value was significantly lower in prostate cancer (PCa) than in benign tissue[6]. However, the reported values of ADC in PCa showed great variations, ranging from 0.98 ± 0.22 x10^{-3} mm^2/s to 1.39 ± 0.23 x10^{-3} mm^2/s. One factor contributing to these variations is the selection of the maximal b-value among the studies. The higher the b-value, the lower the ADC value[7,8]. Also, the ADC value varies with the number of intermediate b-values[9] between 0 and 1000 s/mm^2 and with the inclusion of the b0 value, often discarded to avoid the perfusion effect (pseudo-diffusion).

Another finding shared by all studies is that, despite the significant difference of ADC values between cancer and benign tissue, an overlap could be noted between benign and malignant focal lesions[10]. Lastly, the two parameters used to measure the ADC value, diffusion time (Figure 1) and duration of application of the gradients[11] should theoretically be the same to compare ADC values across patients, but they are currently integrated together into one b-value. As a result, quantitative ADC metrics should be used with caution to better characterize focal prostatic abnormalities. To circumvent this limitation, the only reliable alternative would be for each center to define its own cut-off ADC value to differentiate PCa from benign tissue, according to the local DW protocol and MR platform used.

For example, in our routine practice, the mean ADC value is measured at the upper, mid and lower part of the lesion and the lowest value is the reference value. With regards to score 3 lesions (Table 1), we confirmed that cancer lesions had a lower mean ADC value than benign lesions (0.978 ± 0.146 vs 1.120 ± 0.115 x10^{-3} mm^2/s, p=0.02). The value of the area under the curve (Az) of the ADC value to differentiate PCa from benign tissue was 0.795. A sensitivity (Se) of 89% could be obtained at a cut-off value of 1.080x10^{-3} mm^2/s achieving a specificity (Sp) of 50%. This finding may help for the biopsy decision making in score 3 lesions, allowing for the deferral of 25% of immediate biopsies.

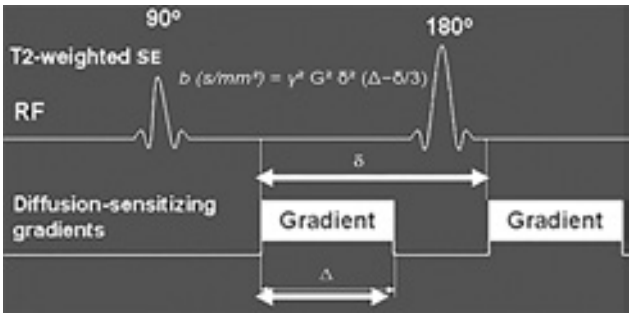


Figure 1: Water Diffusion Metrics (modified from[64]). Two rectangular gradient pulses of equal strength are applied before and after the 180-refocusing pulse of the turbo fast spin echo sequence. δ (diffusion time) is the time interval between the two gradient lobes, and Δ is the overall time interval during which the gradients are applied (gradient duration). The b-value (formula in brackets) is linearly related to Δ, but also to the square of δ. The values should thus be the same in every patient to have a valid comparison of ADC values across patients.

The ADC ratio

The ADC ratio consists of calculating the ratio of the mean tumor ADC value to that of a surrounding reference tissue. This intra-patient normalized ADC may compensate for equipment-related variations and improve the discrepant performance of absolute ADC values. To measure the ADC ratio, a region of interest (ROI) is placed in the contralateral benign PZ, in mirror position to the tumor.

A mean ADC ratio value of around 0.60-0.65 is the most often reported cut-off to differentiate PCa from benign tissue[12]. However, as for ADC metrics, the discriminant value of the ADC ratio showed conflicting results. Some studies[13] reported that the correlation coefficient with the presence of tumor was higher (0.883) for the ADC ratio compared with that obtained when the absolute ADC values were used alone (0.873). Other studies showed the opposite[12] by reporting that for PZ tumor detection the ADC value achieved a significantly higher Az value and specificity than the ADC ratio. With regard to score 3 lesions, our experience (Table 1) showed that the mean value of ADC ratio of tumors was not significantly different from that of benign lesions (0.57 ± 0.07 vs 0.61 ± 0.1). These discrepancies may be due to the fact that the benign PZ

Table 1: ADC metrics and derivates in 41 score 3 lesions (Cornud et al., unpublished data).

	Benign (32)	any Ca (9)	GS 3+3 (4)	GS 3+4 (5)
ADC (x10^{-3} mm^2/s)	1.12 ± 115	0.9 ± 0.136 (p=0.003)	0.937 ± 0.15	1.01 ± 0.013 (p=0.45)
ADC ratio				
Mirror	0.61 ± 0.1	0.57 ± 0.07 (p=0.26)	0 59 ± 0.06	0.56 ± 0.08 (p=0.14)
Whole Prostate	0.72 ± 0.09	0.6 ± 0.06 (p=0.0002)	0.53 ± 0.08	0.63 ± 0.03 (p=0.03)
WL ADC (x10^{-3} mm^2/s)				
Mean	1.2 ± 0.0.155	1.06 ± 0.93 (p=0.02)	1.04 ± 0.59	1.08 ± 117 (p=0.5)
10%	1.08 ± 0.143	0.95 ± 0.15 (p=0.37)	0.93 ± 0.75	0.97 ± 0.19 (p>0.07)
25%	1.17 ± 0.142	0.99 ± 0.11 (p=0.10)	0.97 ± 0.74	1.01 ± 0.15 (p>0.05)
50%	1.17 ± 0.14	1.07 ± 0.106 (p=0.055)	1.04 ± 0.62	1.10 ± 0.13 (p>0.05)
SI ratio				
1500	1.7 ± 0.33	1.8 ± 0.39 (p=0.13)	1.8 ± 0.3	1.9 ± 0.5 (p>0.05)
3000	2.84 ± 0.95	4 ± 1.26 (p=0.005	4.1 ± 1.4	4 ±1.3 (p>0.05
6000	6.49 ± 4.5	15.7 ± 12.7 (p=0.001	18 ± 19	13 ± 6 (p>0.05)

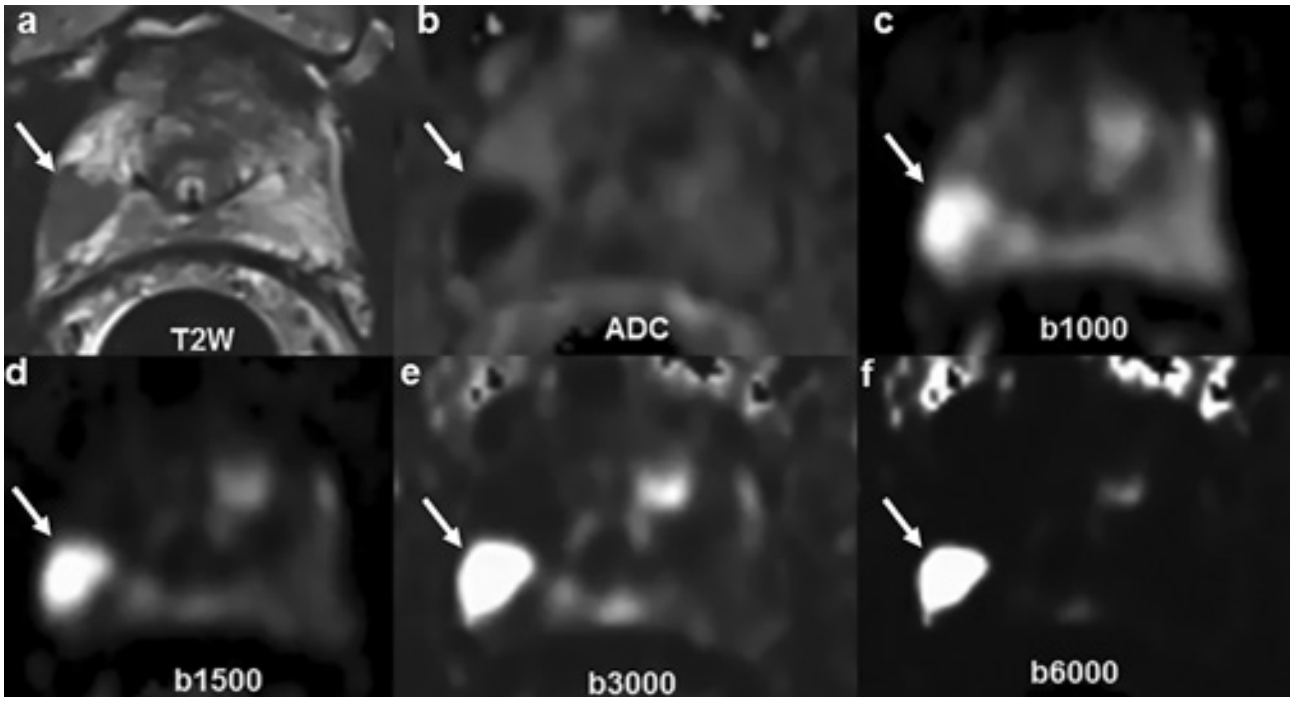


Figure 2: Very high computed b-values in a score 4 lesion. Right focal hypointensity on T2W (arrow, a) in the right lobe, dark on the ADC map (b), extracted from a b-50-500-1000 DW acquisition, and bright on the acquired b1000 images (c). As the computed b-value increases (d,e,f), the benign prostate is more and more suppressed, while the tumor remains bright.patient to have a valid comparison of ADC values across patients.

commonly shows variations of signal intensity related to the frequency of PZ benign changes such as prostatitis, fibrosis or atrophy[12]. As a result, we thought it could be more appropriate to define a more reproducible ROI to average the heterogeneity of the benign prostate (Figures 2 and 3). We thus calculated the Az of the ADC ratio by choosing the rest of the entire surface of the benign prostate, including the PZ and the TZ as the ROI of reference. In score 3 lesions (Table 1), the ADC ratio with this metric was significantly lower in Ca (0.6 ± 0.06) than in benign focal lesions (0.73 ± 0.09) ($p<0.0002$). The Az value was 0.89 and a cut-off value of 0.66 could detect any prostate cancer with a sensitivity of 90% and a specificity of 75% (Table 1).

Whole lesion ADC with values of the 10th, 25th, and 50th percentiles

Recent studies have shown that the prognostic value of more sophisticated ADC metrics derived from whole-lesion histogram assessment[14-17].

Such metrics may also represent an aid for the management decisions in score 3 lesions. A software is required for the segmentation of the lesion by placing a 3D volume of interest involving all slices showing the lesion. Whole-lesion ADC metrics (mean value and mean values determined by the 10th, 25th, and 50th percentiles) are then computed.

These metrics are supposed to provide a more robust assessment of the presence of low ADC values within the lesion than does the absolute minimum ADC value within any single voxel. In score 3 lesions, a study[18] showed that, in naïve biopsy patients, a whole lesion ADC value at the 25th percentile ≤1.04 $x10^{-3}$ mm^2/s achieved a 90% sensitivity and 50% specificity to suspect the presence of a Gleason score (GS) >6 tumor.

Comparison with the accuracy of the mean non-whole lesion ADC value was not available in the article.

In our practice (Table 1), we found that the mean whole-lesion ADC value of score 3 cancer lesions was significantly lower than that of benign lesions. The Az value was 0.76 and a cut-off value of 1.18$x10^{-3}$ mm^2/s could detect any tumor with a sensitivity of 89% and a specificity of 47%. However, the 10th and 25th percentiles were not significantly different between both groups.

Very high b-values images

To increase the conspicuity of tumor foci, the use of computed b-values of 1500 or 2000 s/mm^2 is recommended[19-23]. Computed high b-values images increase diffusion-weighting, allowing for a greater suppression of benign prostate, and thus improve the sensitivity of source DW-MR images for the detection of PCa (Figures 2 and 3).

More recently, several studies have reported a greater contrast between tumor and benign tissue at still higher computed b-values of 2500 to 4000 s/mm^2 [19,24-27], considering that b-values >2000 s/mm^2 can show a continual greater degree of benign tissue suppression. All these studies have evaluated the increase of the tumor conspicuity visually, so that no quantitation has been evaluated to define a cut-off value to differentiate PCa from benign tissue. However, in one of these studies[26], the ratio between the signal intensity of the PZ tumor and the rest of the PZ has been shown to steadily increase as the b-value was increasing, thus potentially defining a quantitative parameter to differentiate PCa from benign lesions. The rationale for such an approach is that computed DWI at very high b-values, up to 6000 s/mm^2, synthetized from measured images with b-values between 0 and 800 s/mm^2, yield a high contrast to noise ratio, because computed values are theoretically noise-free, hence not affected by the noise floor effect due to the non-normal Rician distribution of the noise[28].

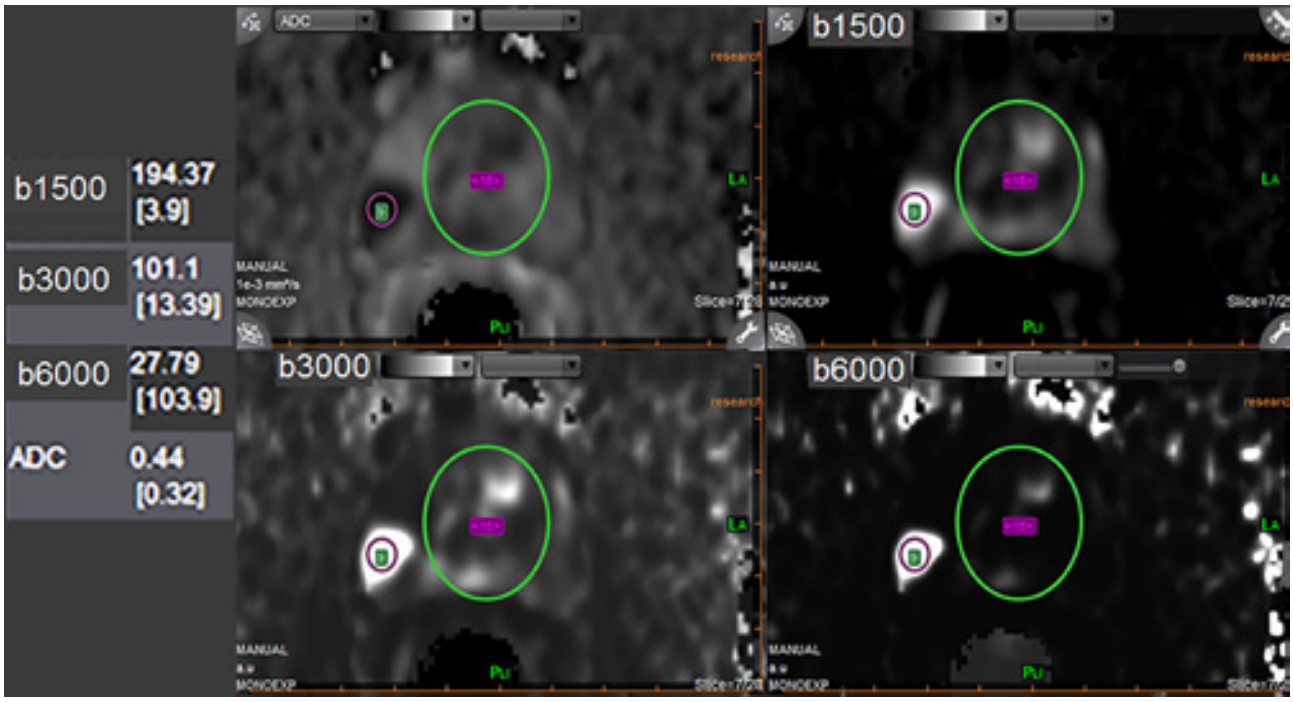


Figure 3: Signal Intensity Ratio metrics (same patient as in Figure 2). A reference ROI is placed on the tumor and a second one on the rest of the benign prostate. The ROIs are automatically propagated to all b-values and to the ADC map. The SI ratios are automatically calculated by the software. The value steadily increases from 4 to 104, as the b-values increase from 1500 to 6000 s/mm². Of note the low value of the ADC (0.44 x10⁻³ mm²/s) and of the ADC ratio (0.32) measured with the rest of the prostate as the reference ROI. Targeted biopsies showed a Gleason score 4+3 tumor with 70% G4.

These metrics can be evaluated using the Bayesian theory which has been successfully applied to improve the performance of ADC metrics[29,30]. This probabilistic approach is used in Olea Sphere® software to calculate more robustly, with regards to the noise level, the ADC value and to synthetize very high b-values.

Quantitative very high b-value DWI may thus represent an adjunct to the ADC map, especially in score 3 lesions, to differentiate PCa from benign tissue, at least in the PZ.

In our practice (Table 1), we studied the Signal Intensity Ratio (SIR) between the lesion and the rest of benign prostate on the same MRI slice including, as for the ADC ratio, the TZ and the PZ. Olea Sphere® software allows for a computation of an array of very high b-values. As shown in Figure 2, the benign prostate is more and more suppressed as the b-value increases and results in an increase of the SIR. With regard to score 3 lesions (Figure 3), we found that the SIR was significantly greater in cancer than in benign lesions at b-3000 (4 ± 1.26 vs 2.84 ± 0.95, p=0,005) and still significantly greater at b-6000 (15.7 ± 12.7 vs 6.49 ± 4.5, p=0,0012), but not at b-1500 s/mm². At b-3000, the value of the Az was 0.78 and a cut-off of 2.7 achieved a sensitivity of 100% and a specificity of 53% for the detection of any cancer. At a b-value of 6000 s/mm², the Az was 0.82 and a cut-off value of 7.6 achieving a sensitivity of 100% and a specificity of 66%, although the difference was not significant with results at a b-value of 3000 s/mm².

Quantitative DWI and assessment of gleason score of PZ cancer

Numerous studies have shown an inverse relationship between the ADC value and the surgical Gleason score of PCa with an overall correlation coefficient which varies from 0.32 (weak correlation) to 0.50 (fair correlation). The ADC value of Gleason 6 tumors is above 1 x10⁻³ mm²/s in all studies[7,17,31-43] but one[44] (range: 1.04-1.3), and is higher than that of Gleason score >7 tumors (range: 0.69-0.88 x10⁻³ mm²/s). All studies share showed a substantial overlap between the different subclasses, as indicated by the high values of reported standard deviations. Similarly, whole-tumor ADC metrics[14,45] showed that the mean and/or the mean 10th percentile ADC values were lower in Gleason 6 vs >6 tumors.

Results of ADC ratio metrics were discrepant, probably for the same reasons as for the diagnostic value of the ADC ratio (see above). Some authors[41,46] found a mean ADC ratio <0.50 in GS>6 tumors vs >0.50 in GS=6 tumors. In another study[47], using an unusual set of acquired b-values (0-800-1600), the Az value was 0.92 (p=0.12) for the ADC value and 0.86 for the ADC ratio (p=0.42), indicating no incremental value of the ADC ratio compared to that of the ADC value.

Several studies aimed to be more accurate and addressed the more specific challenge of intermediate grade tumors (Gleason score 7) which probably represents the true challenge of DW-MRI. Tumor aggressiveness is strongly related to the percent of Gleason grade 4 (%G4) components present within the tumor[48]. Stamey et al[49] demonstrated that biological progression after radical prostatectomy increased for each 10% increment of %G4 and the poorer prognosis of Gleason score 4+3 vs 3+4[50] has been well-established[51].

The accuracy for the detection of the %G4 has been significantly increased these past years thanks to MR-targeted biopsies, but some limitations, namely the detection of small amounts of Gleason grade 4 and the determination of the primary grade of Gleason 7 tumors can still be noted[52] (Table 2). Several studies[7,17,33,35,38,42] compared ADC values of Gleason score 74+3 vs 73+4 and discrepancies could

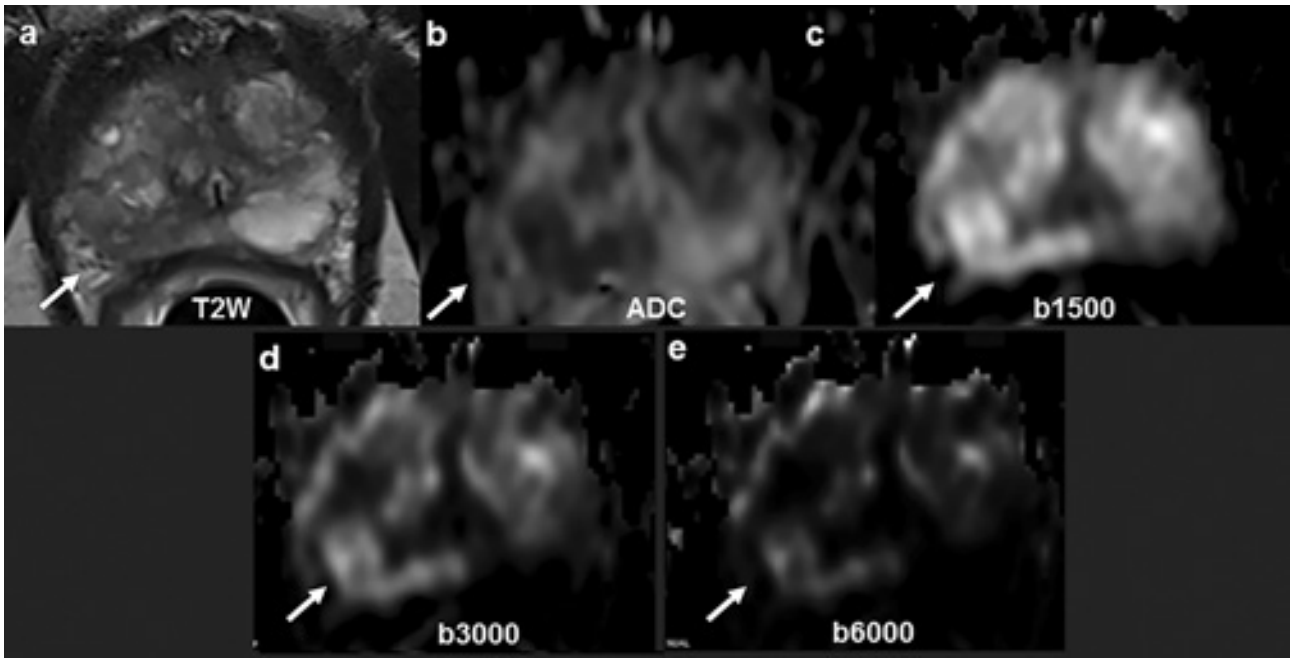


Figure 4: Very high computed b-values in a score 3 lesion. 67 y/o man. PSA: 18 ng/ml. Two series of systematic negative biopsies. Right focal hypointensity on T2W images (arrow, a) in the right lobe, dark on the ADC map (b) and isointense on the acquired b-value of 1500 s/mm2 (c). As the computed b-value increases (d,e), both the benign prostate and the lesion are increasingly suppressed.

be noted. Some authors[17,42] failed to show a significant difference between both groups, while four studies[7,33,35,38] found the difference to be significant. Whole-lesion ADC metrics similarly failed to find a significant difference between the two categories of Gleason Score[17,53].

These discrepancies may be due to the enrollment of score 73+4 tumors with varying amounts of grade 4 across studies. Intuitively, it may indeed be expected that tumors with small amounts of grade 4 (up to 20-25%) have a mean ADC value similar to that of Gleason 6 tumors, because the distribution of grade 4 components is diffuse, making thus impossible to detect an area within the tumor with a more restricted diffusion supposed to contain the Gleason grade 4 (G4) component. Moreover, between 40 and 60% of G4, evaluation of the %G4 may vary across pathologists. It can thus also be expected that, in the range of 40-60 %G4, the ADC value may not be significantly different to differentiate Gleason score 3+4 from 4+3 tumors.

In score 3 lesions, the use of ADC metrics to predict the presence signs of aggressiveness may thus be challenging. Nevertheless, it should be noted that the cancer detection rate of Gleason score >6 lesions in score 3 lesions by MR-targeted biopsies is low. It varies between 0[4] and 8.8 %[18]. Also, in our experience, the percent of Gleason grade 4 observed in score 3 cancer lesions is low, no greater than 20% at surgical histology, similar to that observed in non-visible Gleason score 3+4 tumors, characterized by a low volume and a %G4 not greater than 20%[52]. It may thus be questioned if an immediate diagnosis of these tumors is required as a radical treatment.

In one study[18], a whole-lesion ADC value at the 25th percentile ≤1.04 $x10^{-3}$ mm^2/s achieved a 90% sensitivity and 50% specificity for the detection of GS > 6 tumors. In our experience, the only factor which could discriminate Gleason score 3+4 from Gleason score 3+3 tumors in score 3 lesions was the ADC ratio using the whole benign prostate as the reference ROI (0.53±0.08 vs 0.63±0.03, respectively, p=0.03) (Table 1). The Az value to detect GS 3+4 tumors was 0.8 and a cut-off value of 0.63 provided on the ROC curve a sensitivity of 80% and a specificity of 78% to predict the presence of a >0-20% grade 4 component. Values of the other factors (mean ADC, whole-lesion mean ADC value whatever the percentile, signal intensity ratio whatever the b-value) were not significantly different between both groups.

Table 2: Correlation of the %G4 component of TRUS-MRI image fusion targeted biopsies (TB%G4) with the pathological %G4 component of radical prostatectomy specimen (RP%G4) (from reference [52]). The %G4 detected on TB is upgraded to a higher rate in 15-43% of cases, depending of the %G4 category.

TB % G4 / RP % G4	0% G4 GS6	>0-25% G4 GS 3+4	>25-50% G4 GS 3+4	>50% G4 GS 4+3
0% G4 GS6	45%	4%	4%	0
>0-25% G4 GS 3+4	43%	54%	18%	0
>25-50% G4 GS 3+4	10%	27%	48%	8%
>50% G4 GS 4+3	2%	15%	30%	92%

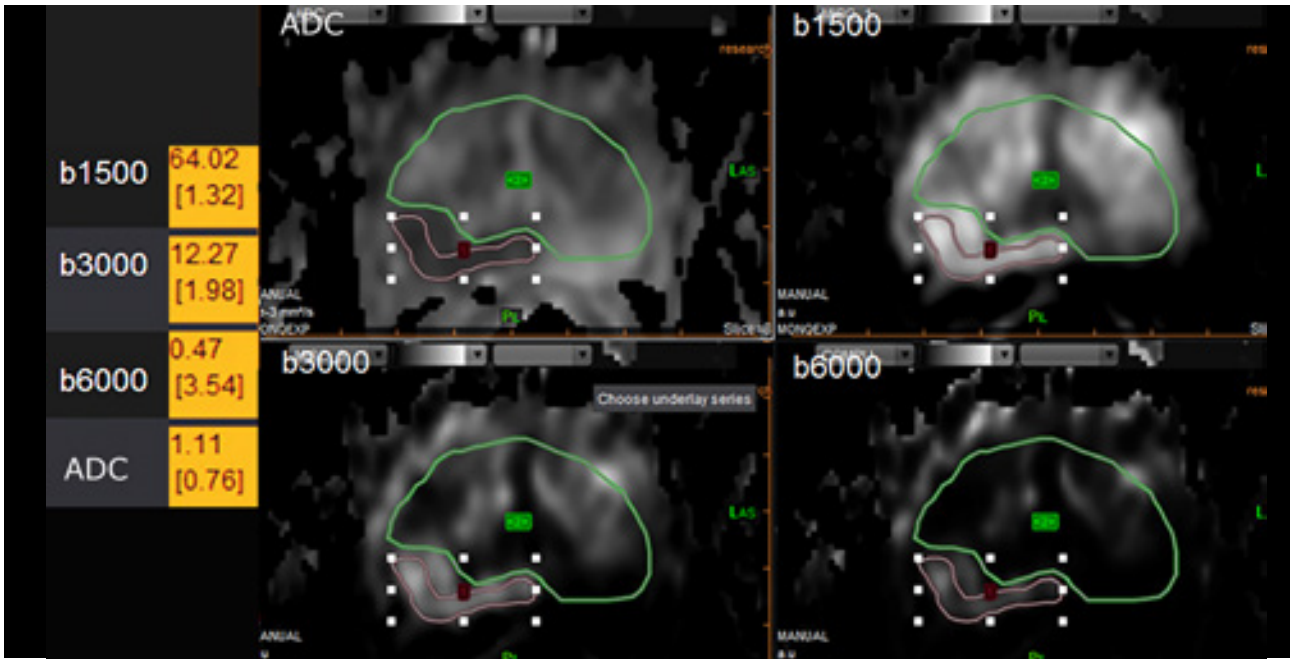


Figure 5: Signal Intensity Ratio metrics (same patient as in Figure 4). The SI ratio is of 2 at b-3000 and of 3.5 at b-6000 s/mm2, suggesting benign tissue. Note however that the value of the ADC (1.1 x10^{-3} mm2/s) and of the ADC ratio (0.76) also suggest benign tissue. Sixty template transperineal biopsies showed benign tissue.

Advanced DW-MRI techniques

Bi-exponential diffusion (IntraVoxel Incoherent Motion, IVIM) or how to separate the perfusion and the diffusion effects in DW-MRI.

In the capillary compartment of the model originally described by Le Bihan et al[54], the movement of water molecules mimics a diffusion process (pseudo-diffusion), evaluated by perfusion parameters (D*, or ADC^{fast}), derived from the weighting by several low b-values (0-100) (Figure 6). D* is represented by the initial portion of the curve which has a steep slope, because of the greater 1H2O distance motion when diffusion gradients are applied.

"D has the highest accuracy to discriminate PCa from benign tissue."

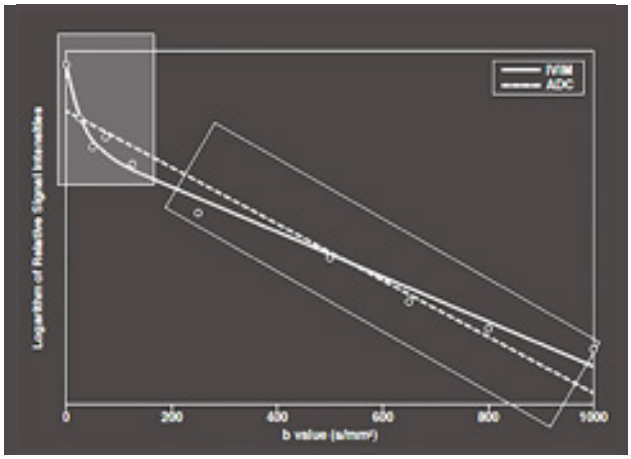


Figure 6: Bi-exponential decay of the DW signal, modified from[65]. The initial portion of the curve is steep for plotted signal intensity values at low b-values (within the rectangular light grey box). However, at higher b-values (dark grey rectangular box), the slope is less steep. The hockey stick shape of the bi-exponential curve provides a better fitting to the acquired DW data than the mono-exponential model used to generate the ADC map (dotted line).

The second part of the curve is evaluated with higher b-values. The slope is less steep and reflects tissue diffusion (D or ADC^{slow}). f corresponds to the blood volume derived from water protons flowing through pseudo-randomly oriented micro-capillaries and has been labelled perfusion fraction in the study by Le Bihan et al[54].
Several studies[55-59] showed that, among the three parameters (D, D* and f), D has the highest accuracy to discriminate PCa from benign tissue, but all the studies showed that D and ADC values performed equally to discriminate tumor from benign tissue (AUC: 0.9). Some studies[56,60] found that the value of D could discriminate low- (Gleason score <7) from high-grade (Gleason score >7) PCa.

The other parameters of the bi-exponential model (D* and f) showed a great variation of values with very large standard deviations and were thus not discriminant between Ca and benign tissue in all studies, but one[60]. The conclusion was that exclusion of this highly variable perfusion component may increase the diagnostic and prognostic values of the D parameter. Our experience at 1.5T with a reusable rectal coil (In Vivo) with a 10 b-values (0,10,20,30,40,50,80,100,500,1000) sequence showed that D and ADC values performed equally (AUC 0.89 and 0.91 respectively). The optimal cut-off value, regardless of the PIRADS score, to differentiate Ca from benign foci was 1070 for the ADC value (Se: 84%, Sp: 83%) and 1190 for the D value (Se: 86%, Sp: 83%).

Thus, although the bi-exponential model may provide a better fitting when multiple small b-values are used, further studies are required to confirm its potential incremental value over that of the mono-exponential model in the detection of PCa. In this regard, a study[61] showed that when measuring the whole lesion value of the ADC and that of D, D performed better, especially the 10th percentile value to differentiate GS6 tumors vs GS>6 tumors.

Kurtosis Diffusion Imaging

Overlap of quantitative ADC values derived from higher and lower grade PCa as well as from benign tissue may be due to another limitation of the mono-exponential DWI-based estimation of ADC, which assumes a Gaussian distribution of the displacements of the water molecules. However, when cellularity increases and restricts water diffusion, displacement of water molecules is assumed to become non Gaussian. The term Kurtosis describes the deviation of a non-Gaussian distribution compared with a Gaussian distribution. Using Diffusion-Kurtosis MRI (DK-MRI), it is possible to quantify this deviation. The Kurtosis is extracted from DW images acquired with a multi-b DW sequence including two b-values above 1000 s/mm² (b1500 and b2000) and may allow for a better differentiation between Ca and benign tissue. A high b-value of about 2000 s/mm² is needed to have a sufficiently large effect on the DW signal when a non Gaussian distribution is tested.

Only few clinical applications of DK-MRI of the prostate have been published. In the initial study[62], K values were higher (0.96 ± 0.24) in Ca than in benign PZ (0.57 ± 0.07) and also higher in Gleason score >6 tumors (1.05 ± 0.26) than in Gleason score 6 tumors (0.89 ± 0.20, p<.001).

The sensitivity of K was greater than that of the ADC for differentiating Ca from benign PZ (93.3% vs 78.5%, p<.001) without loss of specificity (95.7%, p>0.99) and showed a comparable value of the AUC (68.6% vs 51.0%) for differentiating Gleason score 6 tumors from Gleason score >6 tumors.

Interestingly, a second study from another group[63] did not reveal a significant difference between K and standard ADC for the detection of any cancer and of Gleason >6 tumors. The discrepancy between both studies was probably related to the ADC metrics which were extracted, in the first study[62], from the DW-Kurtosis sequence which requires an increased echo time to acquire the b-2000 images (81ms). In this second study[63] a separate standard DWI sequence was used, with a shorter TE (58ms) to calculate the ADC.

It was concluded in the second study that the value of the ADC metrics in a DK sequence may be underestimated. DK-MRI may thus show promise to improve the performance of a standard ADC map, both for diagnosis and assessment of tumor aggressiveness, but further studies are required to reconcile findings of both studies detailed above.

Conclusion

In summary, quantitative DW-MRI of the PZ may improve the specificity of DW-MRI scoring system of the PIRADS. Currently, there is not enough data to suggest that the value of the ADC metrics could be improved by more sophisticated parameters. Whole lesion ADC metrics and advanced DW sequences are under evaluation. However, they are time-consuming and labor intensive. They are thus not yet adapted for routine practice and more automatic workflows are required to incorporate them in workstations. Therefore, it seems useful to suggest simple recommendations.

The first is the use of a standardized protocol with three b-values (the high b-value should not exceed b-1000 s/mm²) and with comparable acquisition parameters across platforms. This step should aid to standardize the ADC value across centers and most probably help to better characterize score 3 or 4 prostatic PZ lesions. It may thus help the biopsy decision making in routine clinical practice in an effort to upgrade or downgrade as much as possible score 3 lesions, to switch to a binary choice which would indicate biopsy or not.

The second recommendation is the use of high and very high computed b-values which increase the conspicuity of PCa and may help to differentiate it from benign tissue. A maximal value of b-3000, if available, has been suggested (26) to visually increase the conspicuity of prostatic tumors.

"The second recommendation is the use of high and very high computed b-values."

The third is to use the rest of the benign prostate as the reference ROI, instead of the contra-lateral PZ, for ADC ratio and signal intensity ratio metrics which may improve the diagnostic accuracy of ADC metrics.

Determination of Gleason score by quantitative DWMRI should take into account the fact that the underestimation rate of Gleason score, which was a major limitation of systematic biopsies, can be considerably decreased if MR-targeted biopsies are routinely used. These biopsies still show limitations to detect small amounts of grade 4 and to accurately predict the primary Gleason grade of score 7 lesions. This information may be an important requirement before including patients in active surveillance or focal therapy protocols. The true challenge of quantitative MRI may thus be to assess if it can predict an upgrade in the %G4 detected on a MR-targeted biopsy. Further research is definitively required to determine if this goal is achievable. //

François Cornud, MD
Radiologist at Cochin hospital; and Professor at Paris-Descartes University, Paris, France.

Thibaut Pierre
Resident in Radiology at Cochin hospital, Paris, France.

Paul Legmann, MD
Head of the Radiology Department at Cochin hospital; and Professor at Paris-Descartes University, Paris, France.

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First publication in Olea Imagein, Issue Number 2, November 2016

The future of Breast Imaging

Aurélie Jalaguier-Coudray, MD
Chief of Women Imaging Unit in Institut Paoli-Calmettes, Marseille.

Could you please explain to our readers the role played by MRI in your daily breast cancer clinical practice, compared to echography and mammography?
Breast MRI is not systematically performed. In case of breast carcinoma, the indications of Breast MRI are detailed in France by the "Haute Autorité de Santé" and in Europe by the EUSOMA group.

In France, a breast MRI must be performed in patients with a histologically-proved breast carcinoma in the following cases:

- Age< 40 years.
- Eligible to a breast conservative surgery with oncoplasty surgery.
- Before a neo adjuvant therapy.
- When the clinical size is discordant with the size in mammography and ultrasounds.

Eusoma group recommends breast MRI in the same situations as above with the adjunction of two indications: first, in case of intraoperative radiotherapy and second, in case of lobular invasive carcinoma, which can be more frequently multifocal and multicentric than ductal carcinoma.

Moreover, breast MRI is a very helpful imaging technique for the radiologists in case of:

- Breast implants: to confirm the absence of intra or extra capsular rupture.
- Patients with high genetic risk: genetic mutations are identified for breast carcinoma. The two most known mutations are BRCA 1 and 2. Patients with this mutation are followed very early (30 y old) with annual breast MRI, mammography and ultrasound.

Among the diffusion imaging techniques, what is your opinion about IVIM to differentiate breast lesions?
Actually, diffusion-weighted imaging is not so used in clinical practice. Diffusion sequences often contain a lot of artifacts. There are some publications about IVIM and characterization of breast tumor but in clinical practice, IVIM is actually not used.

Dynamic contrast-enhanced acquisitions are predictive of malignancy depending on the type of kinetic curves. According to you, what are the future challenges to improve diagnosis with this method? Could a quantitative analysis provide additional information to the qualitative estimate?
Today, to characterize a breast lesion, the margins are the most important criteria to predict a suspicious lesion and perform a breast biopsy. The radiologist focuses more specially on the margins of the lesion, like in mammography and ultrasound.

The kinetic curves can be used but in current practice benign lesion such fibroadenoma could have a wash out (curve 3) like a breast carcinoma and, conversely, an invasive lobular carcinoma could have a progressive enhancement (curve 1) like a benign lesion. As opposed to cervical carcinoma, breast carcinoma has no typical enhancement curve and quantitative analysis.

The use of quantitative analysis in breast MRI has been previously reported to predict the response of neo adjuvant therapy, especially with a MRI after the first cycle of neoadjuvant treatment.

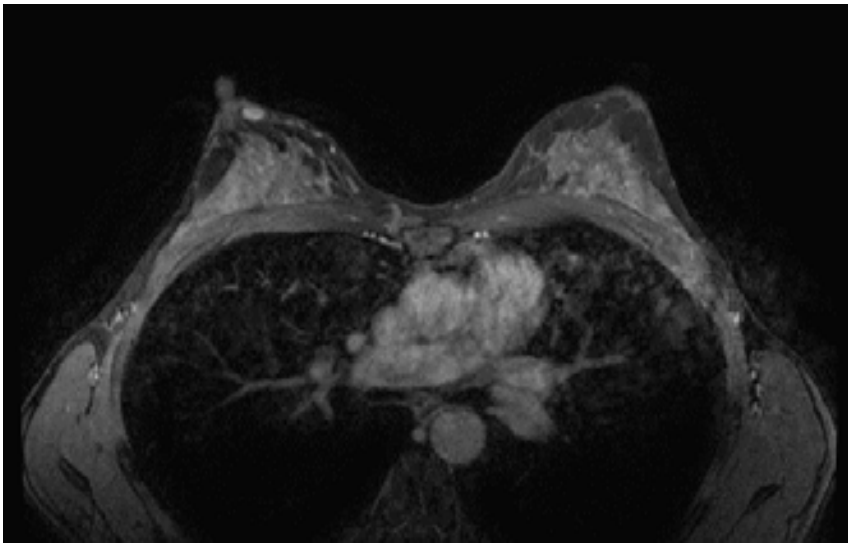


Figure 1: Axial T1 weighted T1 image with fat suppressed showing a retro areolar mass with circumscribed margins, corresponding to a fibroadenoma.

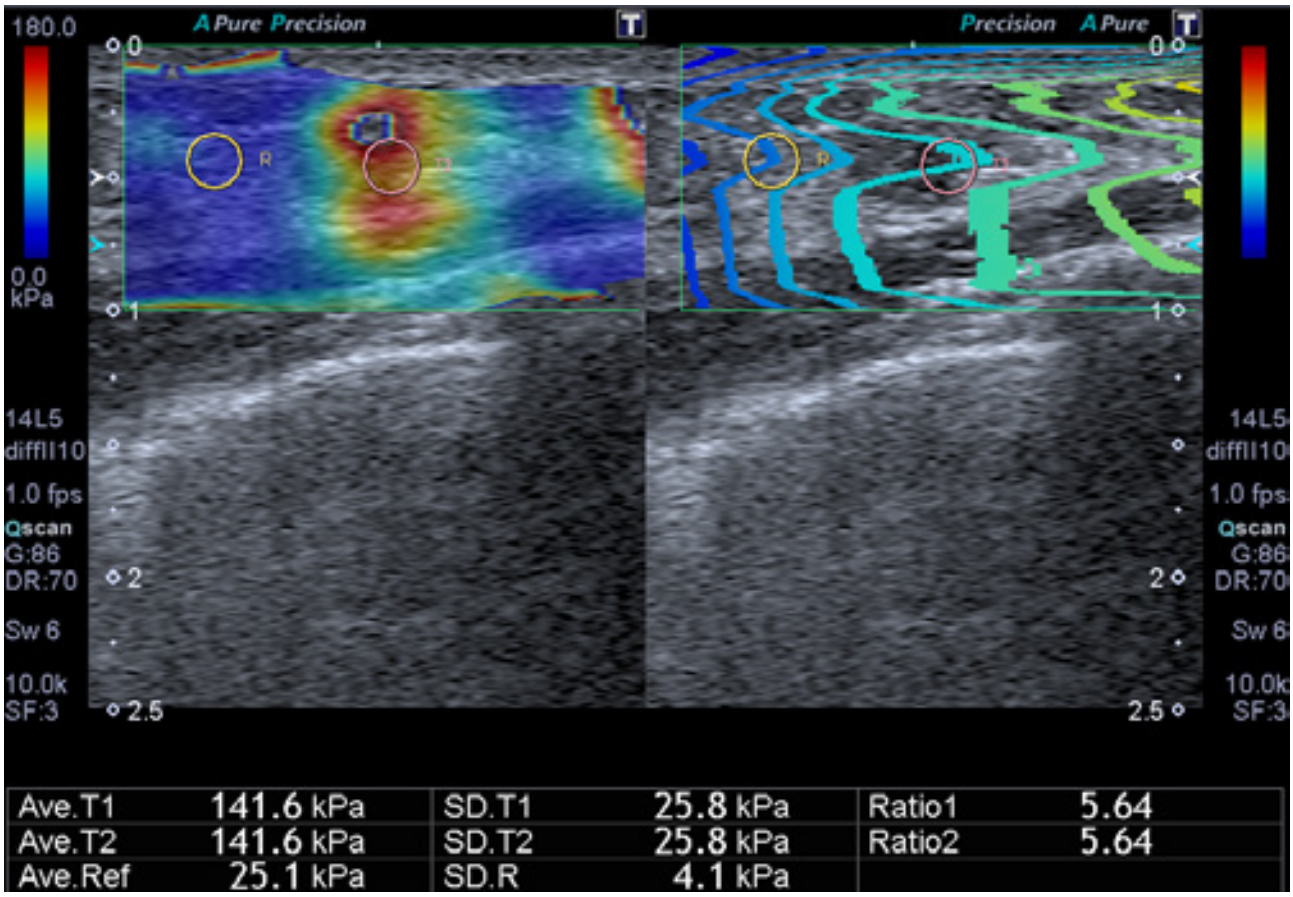


Figure 2: Elastography of a mass rated BIRADS 4.

"In the future, the number of unnecessary breast biopsies must decrease due to an increasing number of breast MRI."

Elastography is a promising technique in the characterization of malignant tumors. Do you believe that it could shortly substitute to biopsy? What would be the benefit for the patient?
No, the studies previously published have not demonstrated that elastography could substitute to breast biopsy. But there is a benefit in the use of elastography, especially in case of intermediary lesion: BIRADS 3 or BIRADS 4.

If a lesion is rated BIRADS 3 with morphological criteria, the use of elastography could upgrade to BIRADS 4 in case of high elasticity. Also, a lesion rated BIRADS 4 on the morphological criteria could be classified as BIRADS 3 with the adjunction of elastography (low elasticity).

Based on your experience, how could MR deliver new data in the near future? Which type of information would you expect?
Breast MRI has a very high sensibility with a low specificity leading to a high number of benign lesion to be detected and biopsied. It will be very helpful for the radiologists to increase the specificity of MRI.

What will MRI look like in the future?
Currently, the use of gadolinium chelate is under debate because of the presence of gadolinium deposits found in the brain. The French radiology society recommends limiting the number of injections in children, young patients. BRCA patients begin their breast MRI at 30 with at least 1 MRI per year. In such patients, a breast MRI without injection of gadolinium will be a real benefit. In the future, and I hope so, the number of unnecessary breast biopsies must decrease due to an increasing number of breast MRI. //

First publication in Olea Imagein, Issue Number 3, March 2017

Diffusion for Breast Application

Kaori Togashi, MD
Professor and Chair of the Department of Diagnostic Imaging and Nuclear Medicine at Kyoto University Graduate School of Medicine, Kyoto, Japan.

Professor Kaori Togashi has been involved in MRI of the female pelvis for more than 30 years. She estimates herself lucky to have started her research at the very early stage of body MRI development. Initially Prof. Togashi was excited to see detailed morphology and experience clinical usefulness of pelvic MRI. Then she gradually recognized the power of MRI beyond morphology; MRI as a functional imaging.

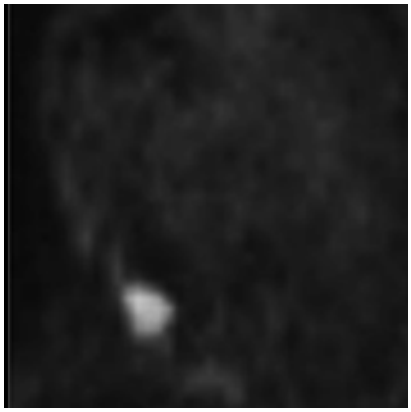
Cine MRI is one of the field of Prof. Togashi's interests in which detailed movie image revealed uterus as a "Dynamic functional organ". After getting promoted to the current position in 2004, she has also been fascinated by the potential of DWI and FDG-PET imaging as other functional imaging modalities.

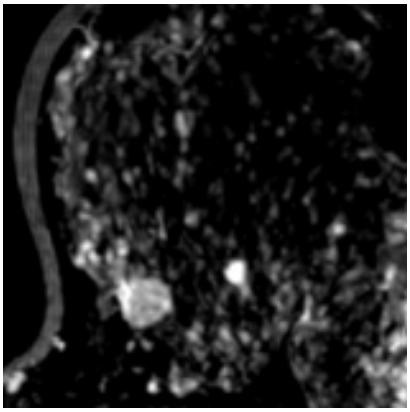
Could you quickly explain what DWI is?
DWI is an image based on diffusion of water in the tissue. In the context of body MRI, the main role of DWI is evaluation of tumor. Along with FDG-PET, DWI is a powerful tool to detect unnoticed small metastasis or to estimate aggressiveness of tumor in various cancers including prostate cancer, uterine cancer, ovarian cancer, liver tumor, and breast cancer.

How do you use it in your daily routine for breast application? How does it help you in your diagnosis process?
In our institution, DWI is now incorporated into almost all of the routine body MR protocols. DWI helps radiologists in detecting known/unknown cancer site and improve our confidence in diagnosing malignancy, particularly when contrast enhanced images show inconclusive results or contrast agent is contraindicated. DWI does not need contrast agent and is, therefore, easy to add on with minimum burden to patients. In addition, apparent diffusion coefficient (ADC) value, a quantitative parameter, provides us with measurable information of the tumor cellularity, composition or structure. For example, ADC value is associated with cellularity and also with proliferative marker in certain types of breast cancer. Outside breasts, DWI sometimes helps in identifying unexpected metastasis to lymph nodes and bones.

Could you briefly present a case study to our readers?
A lady was diagnosed as bilateral fibroadenomas on ultrasound. MRI showed bilateral round circumscribed masses. However, one of the mass showed high signal intensity on DWI (b=1000 s/mm^2 right) with ADC value of 0.9 x 10^{-3} mm^2/s, which was too low for typical fibroadenoma. Pathological examination revealed this lesion as breast cancer. //

"First publication in Olea Imagein, Issue Number 2, November 2016"





Round circumscribed mass pointed out on hypersignal on b-1000 (left) and post-contrast T1-WI (right) series.

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MRI User Meeting 2017

22-23 September 2017

Toshiba Medical proudly announces its 2nd MRI User Meeting in collaboration with Clinica Creu Blanca in Barcelona at Camp Nou, FC Barcelona.

Friday September 22

Men's Health: Prostate MRI

12.00	Early Lunch Buffet
12.50	Welcome

Session 1: Moderator Dr. F. Cornud, Paris, France

13.00-13.15	Introduction into anatomy of prostate, TBD
13.15-13.20	Discussion
13.20-13.35	Technical requirements, by Dr. F. Cornud, Paris, France
13.35-13.40	Discussion
13.40-14.00	PIRADS v2.0, by Dr. T. Durmuş, Berlin, Germany
14.00-14.05	Discussion
14.05-14.25	Gleason score for radiologists, TBD
14.25-14.30	Discussion
14.30-14.50	Pitfalls and non-visible tumors, by Dr. T. Denecke, Berlin, Germany
14.50-14.55	Discussion
14.55 -15.15	*Break*

Session 2: Moderator: Dr. J.C. Vilanova, Girona, Spain

15.15-15.35	A plea for MR-targeted biopsies, by Dr. A. Luna-Alcalá, Jaén, Spain
15.35-15.40	Discussion
15.40-16.00	Staging of Prostate cancer, by Dr. J.C. Vilanova, Girona, Spain
16.00-16.05	Discussion
16.05-16.25	MR-guided focal therapy, by Dr. J.J. Futterer, Nijmegen, the Netherlands
16.25-17.00	Setup Olea Sphere Hands-on / Demo
17.00-18.40	Hands-on / Demo Olea Cases, Cases provided by various speakers
18.40	End of Program

Saturday September 23

Women's Health: Breast MRI

09.00-09.05	Re-opening
09.05-09.35	Technical requirements and Applications Toshiba Medical Spain, Clinical Application
09.35-10.05	Indications, Level of Evidence, Dr. Pau Palañá, Barcelona, Spain
10.05-10.15	Q&A and Open discussion, Dr. M. Sentís i Crivellé, Barcelona, Spain
10.15-10.35	*Break*
10.35-11.05	MRI at High Risk, Dense Breast, Dr. M. Sentís i Crivellé, Barcelona, Spain
11.05-11.35	Advanced MRI Tech: fMRI and contrast, fast MRI SCREENING, Dr. Elsa Pérez, Girona, Spain
11.35-11.45	Q&A and Open discussion, Dr. M. Sentís i Crivellé, Barcelona, Spain
11.45-12.15	Future Developments in Breast MRI, Toshiba Medical / Olea Medical Clinical Application
11.50-12.10	Summary, Final Remarks and Adjournment
12.10	End of Program
12.30	Early Lunch Buffet

Medical/Scientific Chair: Dr. X. Alomar, Clinica Creu Blanca, Barcelona, Spain

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