

Imaging on trial: MRI versus CT

Computed tomography and magnetic resonance imaging are two of the most widely used medical imaging technologies. **Dr Stephen J Pomeranz** and **Richard Taranto** examine the advantages and disadvantages of each method for clinical researchers

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Imaging biomarkers are accepted surrogate endpoints for several therapeutic indications in clinical research and are increasingly forming the basis for regulatory approval. The appropriate clinical trial design and imaging acquisition protocol ensures the accuracy, quality and consistency of imaging data submitted to regulatory agencies.

Two of the most widely used medical imaging technologies are computed tomography (CT) and magnetic resonance imaging (MRI). Both modalities can be used for a variety of indications, therapeutic areas and disease states in biopharmaceutical and medical device trials, and each has unique benefits.

When developing a clinical trial and imaging acquisition protocol, the differences between all available imaging modalities must be considered. In the case of CT and MRI, the differences can be synthesised into three primary categories: scanner technology, appropriateness to anatomical region and safety considerations.

Scanner technology

Both CT and MRI are forms of tomography – the imaging of sections or slices of the body.

CT technology. A CT scanner can be thought of as a rotating unit of X-ray tube with opposing detectors. CT creates a bi-dimensional sectional image of the body and these digitally processed, two-dimensional cross-sections can be used to generate three-dimensional images.

The newest CT scanners contain multiple rows of X-ray detectors. Known as multislice scanners, these units dramatically increase scanning speed and special resolution, and generate volumes of two- and three-dimensional images of individual bones or even the entire skeleton. A CT scanner with 16 X-ray detectors is known as a 16-slice scanner. Developments in scanner technology have meant that by tube modulation and using a fast rotation time of 0.5 sec or less the 16-slice scanner can effectively be used to perform dynamic vascular imaging.

With advancing technology today the multi-row scanners are used for an increasing number of indi-

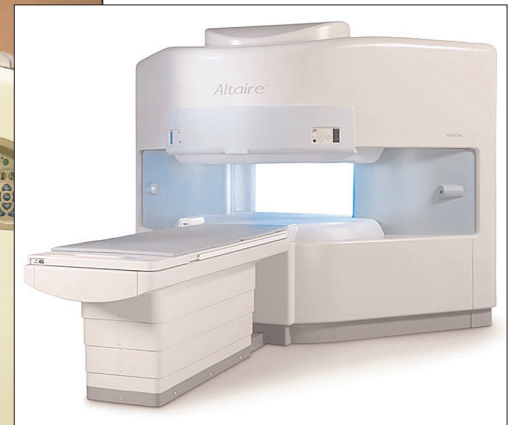
cations for routine examinations. Most major research facilities use 64-slice scanners on a routine clinical basis for cardiovascular evaluation. More advanced technologies include 128- and 256-slice slice scanners; however, only a few of these are currently in use or development for experimental research purposes. The higher speed provided by the 128- and 256-slice scanners is a significant advancement in cardiac imaging, due to its high examination speed, high-image resolution even of the beating heart and reduction in motion artifacts.

In most scanners, the X-ray tube plus the detectors rotate around the patient, who lies on the examination table and is moved through the scanner. The images created appear to be in a helical or spiral orientation and so these are known as helical or spiral multislice scanners. The combination of multislice and spiral technology creates unprecedented speed in patient throughput, which significantly reduces patient examination time and thus decreases patient discomfort during the scan.

The higher-speed CT scanners are, in general, excellent for cardiology applications and for vascular indications because the distribution of an injected contrast agent can be tracked and assessed as it flows through the arteries and veins, showing vessel occlusions or obstructions. Moderate-speed CT scanners remain excellent for other non-cardiovascular applications.

MRI technology. MRI scanners also create two-dimensional images, which then can be processed into three-dimensional images from slices of the body. However, they gather data using a combination of low-frequency radio signals and high-strength magnets. The scanner's powerful magnetic field re-aligns the hydrogen protons of objects placed in it and an image is obtained when additional radio signals are applied to the same body area. At its most primitive, an MRI scanner is basically a microwave and a magnet.

The design and image-resolution power of MRI scanners are connected to the field strength of the magnetic field generated, which is measured in



Left: A closed-bore MRI scanner is similar to a CT scanner. Above: Patients often find open-bore MRI scanners less intimidating.

Tesla. The field strength of MRI scanners can vary between 0.2 and 3.0 Tesla. A field strength of 0.2 Tesla is 2,000 times the earth's gravity; 3.0 Tesla is 300,000 times the earth's gravity. The sophistication of a machine's image resolution and signal strength correspond with an increase in equipment cost.

Most high-field MRI machines are called short-bore or closed-bore scanners. Owing to the technical factors of high-field scanners, the patient must lie down inside a tube, or bore, similar to a CT scanner, but longer and narrower. Patients often find being enclosed in an MRI scanner disconcerting. Therefore machines with lower-field strengths are frequently configured as open scanners, which cause less patient anxiety during the examination. One manufacturer has developed a hybrid open high-strength scanner that is not completely closed.

High-field MRI scanners are necessary for the better image data and the accurate signal required for certain indications, such as spectroscopy, biliary imaging, angiography and other cardiac applications, perfusion imaging and functional imaging. However, the detail level of low-field machines is acceptable in most routine MRI examinations of the brain, extremities, abdomen, pelvis, neck, muscle, orthopaedic and most spine applications.

Safety considerations

In general, both CT and MRI are safe modalities. However, clinical study teams should be aware of safety issues for study participants regarding the radiation used in CT scans, the magnetic fields used by MRI and potential allergic reaction to the imaging contrasts used in both modalities.

Radiation. The primary safety difference between the two modalities relates to the use of radiation for CT scans. The amount of radiation delivered by a CT scan varies based on the examined anatomy, type of examination and slice thickness. MRI scanners, on the other hand, produce no radiation. The

bandwidth and radio waves used by MRI are nearly the same frequency as an FM radio band or microwave oven, and although the magnets used are very powerful, they are considered to be safe for patients, even with repeated use.

CT is a proven and relatively safe technology, but – since it relies on ionising radiation – the same cautions exist as for any other type of X-ray, such as a routine chest X-ray. CT should be used in clinical trials only with discrimination, especially if children or pregnant women are involved, so care must be taken when writing the protocol to ensure appropriate inclusion/exclusion criteria. When this modality is necessary for therapeutic indications, appropriate safety and protection measures must be taken, such as the use of lead blankets to shield sensitive body areas. This precaution is unnecessary for MRI scans.

As people age, their bodies become more radio-resistant. Some organs, such as the lungs and heart, are less radiation-sensitive than others, such as the ovaries, bone marrow and the thyroid gland. But since the amount of radiation involved in a CT scan is significantly higher than that of a single X-ray (depending on the area being examined), and since radiation dose is calculated in organs and by slice per scan, care should be exercised in longitudinal clinical trials, which require multiple, consecutive CT scans.

Magnetic fields. There are no known negative side-effects caused by the application of magnetic fields at clinical strengths. However, MRI is contraindicated for certain patients, including those with defibrillators or who wear a pacemaker. Patients with on-demand pacemakers can undergo an MRI scan if the pacemaker is de-programmed before the exam. Patients with implanted TENS units should also avoid MRI scans.

In MRI applications, patients should remove metal objects, such as jewellery. Eye make-up, which contains metallic particles, should be avoided too. Some tattoos that include iron-based

colour particles may get uncomfortably hot during the time inside the magnetic field. Most patients who have metal inside the body are safe to scan, including those with heart valves, surgical clips, wires, implants, joint or ear prostheses – even most bullets. Notable exceptions include metal that is imbedded deep in the eye. The reason for this is that metal parts will move during the examination, owing to the fast, repetitive alignment and re-alignment of magnetic fields and, due to friction, they may become hot or cause tissue damage. Metallic, ferromagnetic articles such as pacemakers make MRI scans completely unsuitable, as mentioned above.

Contrast. Both modalities may require the use of intravenously injected contrast agents, but much less commonly with MRI. CT requires an iodine-based contrast agent; MRI scans use a gadolinium-based contrast agent. In both instances the intravenous contrast allows better differentiation between tissues with low and higher blood flow, which helps to show inflammatory changes or tumour lesions. In the vast majority of CT and MRI cases, contrast agents can be safely used. Very occasionally, however, the patient may be allergic to the iodine-based contrast used in CT scans. Gadolinium reactions are even rarer – fewer than one in a million patients experience a severe allergic reaction to the MRI contrast.

In general, the safety of imaging contrasts has increased in the past decade. However, an iodine load is more toxic to some patients, for example those with impaired kidney function, than a gadolinium load, especially because a lower volume of contrast is required for MRI (10–40 cc) than for CT (100 cc). Therefore, MRI is generally a safer option for patients with renal insufficiency and some heart conditions, and those with a known allergic reaction to iodine-based contrast media.

Anatomy and imaging

Because of their respective technologies for producing images, CT and MRI may be indicated for different anatomical regions. Although in many instances the two modalities are interchangeable, decisions as to which modality is indicated for a clinical trial will depend chiefly on the density of the anatomical area being examined.

CT indications. In X-ray technology, an image is created when ionised radiation passing through the body is altered before reaching the X-ray film or digital detector by tissue or organs with different densities, such as muscles and bones. Therefore, X-ray-based modalities such as CT are particularly useful in detecting pathologies of tissues with different X-ray absorption characteristics and density.

Fatty areas and air do not absorb X-rays and as such do not block them from reaching the detector, consequently these will appear black on a CT scan.

Dense structures such as bones absorb X-rays and will appear white. CT scans are not ideal for imaging soft tissues such as muscles, joints or brain, but are perfect for detecting air, gas or calcium. CT provides very good spatial resolution, that is the ability to distinguish between two separate structures that are very close together.

CT also offers excellent image quality of the surface portion of bones so it is useful in trauma and orthopaedic indications. For example, CT has craniofacial applications including evaluation of the skull or the base of the skull; facial and skull fractures and deformities; dental, jaw, sinus, and nasal cavity deformities or tumours; the middle ear; dental implants; detection of intracranial pressure; or to study a cerebral shunt. In osteoporosis and bone mineral density studies, CT is sometimes used alongside DEXA scanning. Although DEXA has been the gold standard for studying bone density and strength, it can be more expensive.

CT scans are also preferred for examining the brain, lungs, chest and bowel. It is excellent for studying acute and chronic lung diseases such as pneumonia, lung cancer, emphysema and fibrosis. It can also detect the presence of a blood clot in the veins of the lungs.

Abdominal conditions such as acute abdominal pain, kidney and urinary stones, appendicitis, pancreatic, diverticulitis and abdominal cancer can be examined and measured with CT. For studies of the stomach, bowel and colon, CT with an orally or rectally administered gas or contrast may be indicated. Again, CT is not the modality of choice for studying the pelvis, due to its use of X-rays.

Solid organs such as the liver, pancreas, or kidneys can be effectively evaluated with CT or MRI, but MRI may be more sensitive and specific to answer certain questions in these solid organs.

MRI indications. The magnetic field technology used by MRI scanners is better suited for the study of soft tissue or non-calcified tissues. MRI technology is best when used to distinguish between soft tissue pathologies, especially inflammations and also solid tumours. It is far superior to CT in the evaluation of cartilage in joints and muscles and tendons in extremities. MRI's spatial resolution is not as good as that of CT, but its contrast resolution – the ability to distinguish differences between similar but not identical tissues – is significantly better.

For oncology studies, MRI and CT are appropriate modalities for identifying and measuring masses and tumours. MRI is particularly useful in examining masses and tumours in the liver and pancreas, and the gallbladder and biliary systems, often without intravenous contrast. In certain conditions, MRI can be used to evaluate breast tissue instead of mammography, or as an additional evaluation method. Breast masses in patients with extremely dense breast tissue are easier to see when breast MRI is used instead of X-ray mammography.

As a substitute for more invasive diagnostic tests, or when CT would not be suitable because of radiation or contrast risks, MRI can be used for evaluating heart function and diseases of the coronary artery, as well as other arterial diseases and abnormalities, including stenosis and aneurysm. MRI angiography is used frequently to evaluate coronary, carotid, brain, thoracic, abdominal, renal and leg arteries for clots, obstructions or narrowing. For vascular problems, MRI venography is similarly used to image veins.


MRI is the best modality for studying diseases involving brain and spinal cord tissue, including multiple sclerosis and other demyelinating diseases, brain injuries and haemorrhages, and brain tumours. A technique called MRI spectrography that measures the brain's chemical activity is useful for examining Alzheimer's disease and other dementias, brain tumours, metabolic brain diseases and congenital and hereditary brain diseases.

MRI is the preferred test for almost all spine indications and can be used as a research tool in osteoporosis, especially osteoporotic insufficiency fractures.

Conclusions

CT and MRI imaging are both technologically advanced and safe modalities that have been used with success in the analysis of surrogate biomarkers for multiple clinical trials. Both modalities

have distinct advantages, and some disadvantages, which should be considered when designing the trial and developing the acquisition protocol. Clinical study teams should take into account the differences in technology, safety issues and the anatomical area under study early in the planning phase. Understanding how each modality works is critical in designing a successful clinical trial.

Another important factor for study planning is the financial reimbursement for these exams as part of a clinical trial. Especially when the trial examinations are not following a routine standard of care imaging, schedule health insurances are reluctant to cover the cost involved with research. 

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