Images: © MR Solutions

Figure 1: An operator uses a preclinical MRI sytstem

A View to Succeed

The preclinical imaging market is undergoing a transformation – new, compact scanning systems allow for simplicity of use, a more effective workflow and seamless integration of multiple imaging modalities. With the latest technology offering advanced capability, the future looks bright for researchers

David Taylor at MR Solutions

The preclinical imaging market is evolving so rapidly that there are now systems available which can completely transform the sector. Today's systems can offer multi-modality capability within a compact machine.

The first commercially available, cryogen-free, three tesla (T) preclinical magnetic resonance imaging (MRI) scanners became available in 2012. Being cryogen-free, they have the advantage of no longer needing the cumbersome helium cooling jacket and emergency venting equipment necessary to let out helium, should the internal magnet quench.

This also means that the building works associated with older technology are no longer required for two reasons: firstly, a more compact system allows transportation and movement into the laboratory on wheels; and secondly, it is no longer essential to build a screened room or Faraday cage, or to construct floor reinforcements for heavy equipment.

All of these changes have become possible thanks to the elimination of the liquid helium cooling system, by using a new magnet design incorporating superconducting wire. This enables the use of a standard low-temperature cryocooler to cool the magnet to four degrees kelvin (K) (-269°C) – which is necessary to achieve superconductivity.

Following the introduction of the scanner, the 7T became available in 2014, and the 4.7T in 2015. These have bore diameters of between 17cm and 31cm.

Modern Advantages

The latest preclinical scanners also include variable fields of operation, higher intrinsic magnetic field homogeneity, larger fields of view (FOV), an elliptical shape to better fit the subject, and automatic

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field ramping. Improved imaging has also been made possible by optimising the magnet performance.

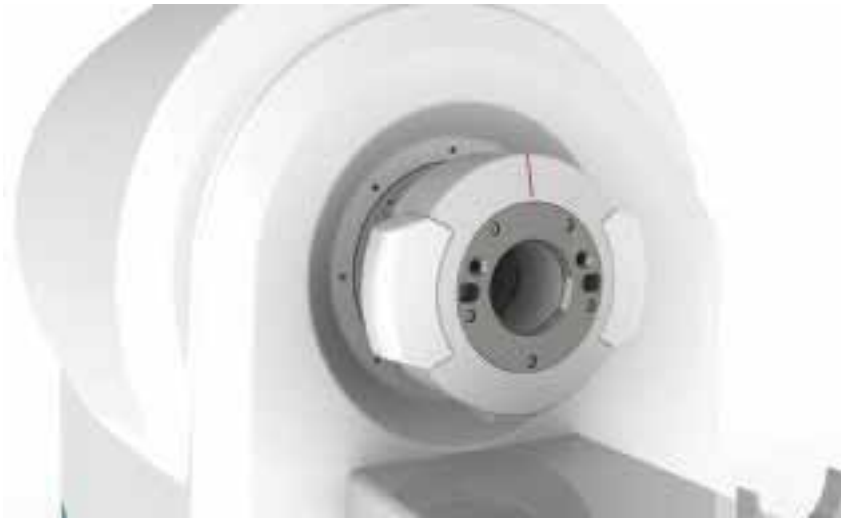
MRI preclinical scanning technology can be used in an array of applications, including neurobiological research – for instance, epilepsy or brain and spine imaging – cardiovascular research; embryology imaging to define development of the embryo; nephrology; full body imaging; organ imaging; morphological imaging; cancer research and a range of other applications.

Cryogen-free scanners may have Faraday cages built into the casing with a solenoid to reduce the stray magnetic field to a few centimetres. This means that the scanner can be placed alongside other preclinical imaging systems. The MRI scanner, traditionally isolated in its own room, no longer interferes with other technology in the lab, and can be used safely in close proximity to other imaging modalities, such as X-ray computed tomography (CT), positron emission tomography (PET) and single-photon emission computerised tomography (SPECT). As a result, MRI scanners can now be placed in Class 3 and 4 labs.

Advances in imaging research bring further opportunities that could completely change the diagnostic process in preclinical research, resulting in quicker diagnoses, pharmaceutical development and treatments. Productivity should increase as imaging is far simpler and faster with multi-modality systems.

PET-MRI systems can now be much more compact, following the implementation of silicon photomultipliers built into the PET – these are either inserted into an MRI system or clipped on at the front. This has meant a smaller, robust system to take the place of larger predecessors, which were often so big that they were difficult to move around. The new PET can simply be unclipped and carried between rooms.

Figure 2: The clip-on MRS-SPECT for small animal imaging is based on multi-pinhole technology, allowing for high resolution and high sensitivity imaging



Multi-Modality Techniques

Researchers can use multi-modality technology to obtain results with different imaging techniques either separately, in sequence, or simultaneously. This includes PET-MRI and SPECT-MRI imaging, where PET or SPECT are simple to clip on, or can be inserted into the magnet. This provides state-of-the-art three-dimensional (3D) SPECT or PET images which can be registered with the MRI images to deliver anatomical-functional combined capability.

Other techniques, such as optical and CT imaging, are also possible. Multi-modality imaging looks likely to become the norm for the study of anatomy, bio-distribution, efficacy, safety and kinetics within the same anatomical context.

Molecular research can be performed using SPECT, PET and optical scanning technology. SPECT uses radioisotopes to capture images from a rotating camera. Changing energy radioisotopes to various target areas can be carried out simultaneously to provide several different molecular images, making SPECT useful in cancer research.

PET, on the other hand, relies on positron-emitting-bound biological molecules that are injected into the living animal. The PET machine has sensors on opposite sides of the scanning technology, which pick up rays emitted from the body and interprets these as images. PET is also used in cancer research, although scientists need to be aware that the radiation required for PET, and indeed SPECT, can affect the tumour size shown. Therefore, different scanning technologies may be required for improved analysis.

Optical imaging uses light from an external source with the signals captured by cameras cooled to up to -150°C. This type of imaging is quick and easily performed, and relatively inexpensive compared with many other imaging modalities. However, optical imaging is only capable of showing pictures of a limited depth, which may be as small as a few millimetres.

CT scanning provides a series of X-rays around a subject placed within the machine. Compared to standard X-rays, CT scanning results in a series of two-dimensional images that can be combined into 3D images. This technology provides excellent image resolution, which can be increased with the use of contrast agents. However, the radiation emitted often means that its use is unfeasible, particularly in labs where small animals are being used for research. The radiation levels may be detrimental to the animal, and results could be adversely affected.

In terms of imaging performance, MRI preclinical scanners now have far greater capability than their older, larger counterparts. The latest software allows for simplicity of use, a smoother workflow and seamless integration of imaging modalities. High-resolution imaging can be easily acquired and analysed, and the resulting data exported.

Updating Older Systems

Where labs have old preclinical scanners, these can be upgraded to provide scanning capability to the standard of today's modern MRI technology. The original magnet can be refitted with new electronics and the spectrometer updated to the latest model, providing superior soft tissue contrast and molecular imaging capabilities. As long as the magnet is intact, the scanners can have a refit – depending on their tesla power – to provide today's scanning functionality. The cost of this varies, but will always be far less expensive than buying a new preclinical machine.

Figure 3: A 7T, cryogen-free, preclinical MRI system

New Technologies

Many MRI applications are limited by low sensitivity. Attempts to overcome this have focused on the use of stronger magnetic fields – however, the gains achieved have been relatively small, and the increase in the magnetic field leads to other technical challenges. Recently, the development of techniques given the umbrella term 'hyperpolarisation' have been billed as a potential solution. Hyperpolarisation approaches increase the signal for short periods of time, allowing for improved imaging ability.

Hyperpolarisation is achieved by placing carbon-13 (^{13}C) in a polariser that maintains a very low temperature (<4K) in a high magnetic field (<3T). The ^{13}C nuclei are polarised by more than 50% – thousands of times greater than with conventional techniques. MRI systems must be optimised to image ^{13}C metabolic activity to take advantage of this and, as the excess polarisation recovers, there is a need for real-time metabolic imaging with fast imaging sequences.

Where Next?

Developments in *in vivo* optical imaging technology will allow for the examination of the interior of a sedated animal, down to a cellular level of up to 1,000 times magnification. Furthermore, new scientific analysis software will facilitate optical microscopy of small animal subjects for preclinical research without having to carry out a dissection.

The other major path will centre on encouraging both regulators and the pharmaceutical industry to incorporate preclinical image scanning into a legal framework. Scanning technologies are gradually being applied to developmental toxicology studies in drug development to determine potential compound toxicity. Although most of these are conducted in a non-regulatory setting, there is interest in performing these imaging studies under applicable legislation – for example, Good Laboratory Practices – to support future decisions concerning drug safety.

Preclinical imaging is at an exciting stage and seeing significant market growth, much of which is down to improved imaging capability due to multi-modality technology. Further developments are reaching the market all the time, helping researchers to provide far better results. We will have to wait and see what comes next.

About the author

David Taylor is Chief Executive Officer at MR Solutions. He holds a PhD in Physics, an MBA, and has been leading cutting-edge MRI companies for 30 years. In 2012, David developed the world's first commercially available, helium-free, 3T preclinical bench top MRI scanner, followed by the more powerful 7T range last year. He has now developed a series of preclinical multi-modality MRI scanners with three different bore diameter sizes.
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