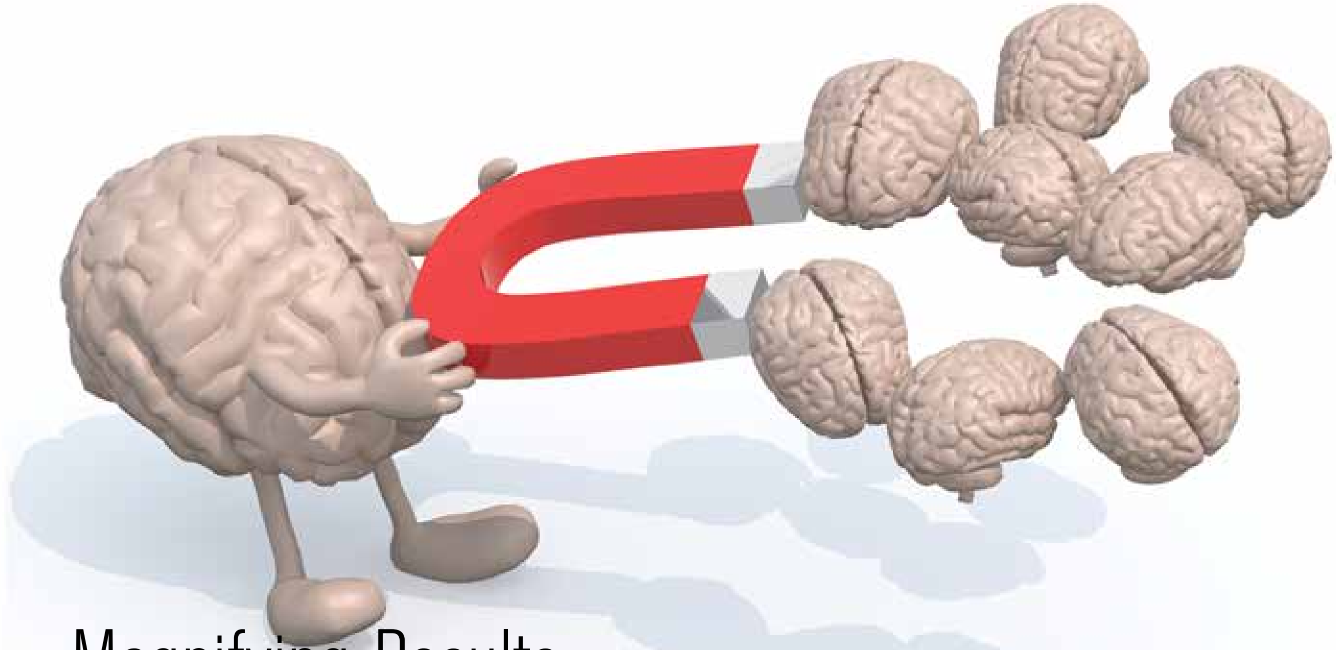

Magnifying Results:
Preclinical Tech Advances Disease Understanding

Advances in MRI equipment are increasing the quality and range of preclinical research in laboratories.

Preclinical scanning has changed radically in the last few years, thanks to new capabilities, advanced technology and steps toward the development of standards that will allow the use of imaging data in regulatory submissions. Three recent developments really drive that point home—high-powered MRI scanners (3 and 7 T) that no longer require cryogen cooling jackets, multi-modality screening and hyperpolarization.

One of the biggest breakthroughs in preclinical scanning has been the development of commercial cryogen-free scanners, presently up to 7 T. This development does away with not only the large cooling jacket, but also the compulsory emergency venting apparatus. This apparatus is necessary should the magnet “quench” (a quench occurs when the magnet becomes non-superconducting). It heats rapidly, causing the liquid helium coolant to expand by 600 times, presenting an asphyxiation hazard to operators by displacing breathable air. This venting system is not only a significant extra cost, but usually necessitates extensive building alterations.

For example, having done away

with the cooling jacket, industry provider MR Solutions was able to incorporate a Faraday cage into the cover, and with an extra solenoid, successfully reduced the stray magnetic field from meters to centimeters. This means that an MRI scanner, traditionally isolated in its own room, no longer interferes with other technology in the laboratory, and can be used safely in close proximity to other imaging modalities, such as X-ray CT, positron emission tomography (PET) and single photon emission computed tomography (SPECT). As a result, MRI scanners up to 7 T can now be placed in the laboratory, including class 3 and 4 laboratories. Not only has this improvement dramatically reduced the cost of a scanner, but it has also reduced running costs as there is no longer a need for helium. Helium, which has to be regularly topped off in a traditional MRI scanner, is becoming increasingly scarce, so the price continues to rise. This is no longer a concern.

With soft tissue contrasting and high spatial resolution, cryogen-free machines provide researchers with much better data, as well as reduced transfer time between scanning technologies in the same room, which avoids differing analysis due to time delays.

Cryogen-free MRI systems enable a broad range of applications, offering superior soft tissue contrast and high spatial resolution.

Multi-modality scanning

Researchers nowadays are demanding multi-modality technology for a number of anatomical and molecular applications, including MRI, clip-on SPECT, PET (either clip-on or built-in), and optical and CT scanning. Currently, separate machines are used for each different technique, but that will change in the future as industry experts continue to develop an increasingly wide range of scanners capable of imaging in different modes. This not only brings down the price, but also offers a scanner that can provide a much wider range of data, which can be combined to provide insight that was previously unattainable.

For example, molecular research can be performed using SPECT, PET and optical scanning technology. SPECT uses rotating sensors to capture images of the distribution of radioisotopes. Combinations of radioisotopes to target different areas can be used simultaneously to provide several different molecular images, which leads to the wide use of SPECT in cancer research.

Meanwhile, PET provides imaging using positron-emitting-bound biological molecules, which are injected into a living animal. Where the positrons meet electrons in surrounding tissue, pairs of gamma rays are emitted in opposite directions. The PET machine has sensors on opposite sides of the device that pick up these rays and interpret them as images. Lastly, optical imaging relies on light from an external light source, with the light signals captured by cameras cooled up to −150 C. This type of imaging can be quickly and easily performed and is relatively inexpensive compared with many other imaging modalities. However, optical imaging depth capability may be limited to a few millimeters.

The MRI scanner will likely remain at the center of these advancements, particularly with the development of new applications, software and new reagents that considerably extend the imaging capabilities of a scanner.

Hyperpolarization

Many MRI applications are limited by low sensitivity. Attempts to overcome this have focused on the use of stronger magnetic fields; however the gains that were achieved were relatively small and the increase of the magnetic field leads to a number of other technical challenges. Recently, the development of techniques that have been given the umbrella term "hyperpolarization" have been billed as a potential solution. Hyperpolarization techniques increase the signal for short periods of time, which allow for improved imaging ability.

Hyperpolarization is achieved by placing the 13C in a polarizer that maintains a very low temperature (<4 k) in a high magnetic field (<3.0 T). The 13C nuclei are polarized by

Agent Innovation Makes MRIs More Effective, Less Toxic

In addition to the future developments David Taylor writes about, a life sciences startup company in India may possess the key to improved MRI results.

Based on Purdue Univ. technology, Aten Biotherapeutics is developing controlled-release imaging agents that allow for longer, safer imaging sessions. Currently, imaging agents, which are small molecules that improve the contract of MRIs, are cleared rapidly through the kidney, holding an imaging session to a maximum of 15 minutes—which is not long enough to image for tumors or cardiovascular problems. And due to the toxicity of the agents, a second dosage often cannot be administered.

Aten's less-toxic imaging agents, however, can stay in the body's circulation for a longer period of time.

"This leads to improved MR imaging," says David Thompson, President of Aten, and a chemistry professor at Purdue. "Agents are released in a slower, more controlled fashion. This leads to a lower concentration requirement for capturing an MR image. The lower concentration of the imaging agent, combined with its longer circulation and degradation into non-toxic byproducts, could potentially lower the risk of long MR imaging procedures."

Aten Biotherapeutics has already received a first round of investments, along with several SBIR grants in India. The company is actively cultivating industry partnerships as it continues clinical testing and generating data. Aten Biotherapeutics is also developing a first-in-class therapeutic for the orphan disease Niemann-Pick Type C, which presents as a progressive neurological disease and eventual total cognitive decline.

Michelle Taylor, Editor-in-Chief

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A clip-on SPECT module enables multi-modality scanning for enhanced results.

more than 50 percent–thousands of times more than with conventional techniques. MRI systems must be optimized to image 13C metabolic activity to take advantage of this. Also, as the excess polarization recovers in time, there is a need for real-time metabolic imaging with fast imaging sequences.

Laboratories will increasingly find that there are new ways to work on much more complex projects with multi-modality systems that have the capability of conducting not only different but enhanced imaging studies, either simultaneously or separately. And the results will be far more likely to attain the rapid approval of regulatory authorities.

This is a revolutionary time for preclinical scanning with all these new, enhanced technologies. The customization of the technology and the development of specific applications will give preclinical scanners a more important role in the advancement of our understanding of diseases and the development of more effective treatments. ●

David Taylor, Founder and CEO, MR Solutions