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Editorial - Preclinical MRI in Portugal: Building the Bridge to Clinical Translation

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Magnetic resonance imaging (MRI) has transformed modern medicine. Multi-parametric characterization of tissue morphology, microstructure, perfusion, metabolism, and function provides unique non-invasive tools that are routinely used to guide patient management. What is less commonly known is that many of the major advances in MRI are first conceived, developed, and validated in the preclinical setting. Before these new methodologies become available in clinical centers, they are refined in experimental models where imaging findings can be directly compared with histology, molecular biology techniques, and disease mechanisms.

This close interaction between fundamental science and imaging technology makes preclinical MRI an essential driver of clinical innovation. Experimental models provide controlled environments for developing imaging biomarkers capable of characterizing tissue morphology, microstructure, perfusion, and metabolism, with a level of validation impossible to achieve in humans alone. At the same time, preclinical MRI faces an inherent translational challenge. Animal models cannot fully reproduce the complexity of human diseases, while differences in magnetic field strength, gradient performance, radiofrequency hardware, and pulse sequence implementation often require substantial methodological adaptation before successful clinical translation.

Portugal has witnessed a remarkable transformation in this field over the last decade. What began as isolated initiatives has evolved into a complementary national ecosystem spanning technological innovation, biological validation, and clinical translation.

A major milestone was the installation of Portugal's first horizontal 9.4 Tesla preclinical MRI scanner at the Institute for Nuclear Sciences Applied to Health (ICNAS), University of Coimbra, under the leadership of Dr. Miguel Castelo-Branco. This infrastructure enabled pioneering neuroimaging studies in rodent models of neurodevelopmental disorders (Petrella et al., 2016), and continues to demonstrate the value of experimental MRI for understanding disease mechanisms beyond behavioral phenotyping, e.g. in autism spectrum disorders (Pais et al., 2025).

The subsequent establishment of the preclinical MRI center at the Champalimaud Foundation, led by Dr. Noam Shemesh, expanded Portugal's international visibility in MRI methodology. Today, the center hosts a 1 Tesla benchtop scanner and three ultra-high-field systems – a 9.4 Tesla horizontal scanner, a 16.4 Tesla vertical system, and the world's first 18 Tesla horizontal MRI scanner – all equipped with cryogenic radiofrequency coils that substantially enhance sensitivity and spatial resolution. These unique capabilities have enabled the development of innovative approaches for probing tissue microstructure, metabolism, and function. Applications ranging from stroke (Alves et al., 2022) to neuro-oncology (Simoes et al., 2025) and pancreatic cancer (Bilreiro et al., 2025) illustrate how methodological advances developed in experimental disease models can reveal imaging biomarkers with clear potential for future clinical implementation.

Paradoxically, however, the extraordinary performance of ultra-high-field MRI also highlights one of the principal obstacles to translation. Most clinical scanners operate at 1.5 or 3 Tesla, where fundamental differences in tissue relaxation and hardware capabilities limit the direct translation of methods developed at 9.4 Tesla and above. Imaging biomarkers developed under ultra-high-field conditions therefore require careful adaptation before they can become clinically useful. Bridging this gap is one of the most important objectives of translational MRI research.

Within this context, the recent establishment of the Preclinical MRI laboratory at i3S introduces an important new dimension to the Portuguese landscape. Built around a new-generation horizontal 3 Tesla preclinical MRI system equipped with a cryogenic radiofrequency coil, the laboratory was specifically conceived to operate under acquisition conditions much closer to those encountered in clinical practice. Rather than replacing ultra-high-field systems, it complements them by providing an intermediate step between methodological development and clinical implementation.

The potential of this approach is demonstrated in vivo in the mouse brain: advanced diffusion MRI enables quantitative mapping of tissue microstructure, including fiber orientation and multi-compartment models mapping cellular geometries and sizes, while high-quality magnetic resonance spectroscopy characterizes regional brain metabolism (Figure 1). Together, these complementary techniques provide a comprehensive assessment of anatomy, microstructure and metabolism within a single examination, establishing a translational framework currently being applied to disease models, including neurological disorders and cancer.

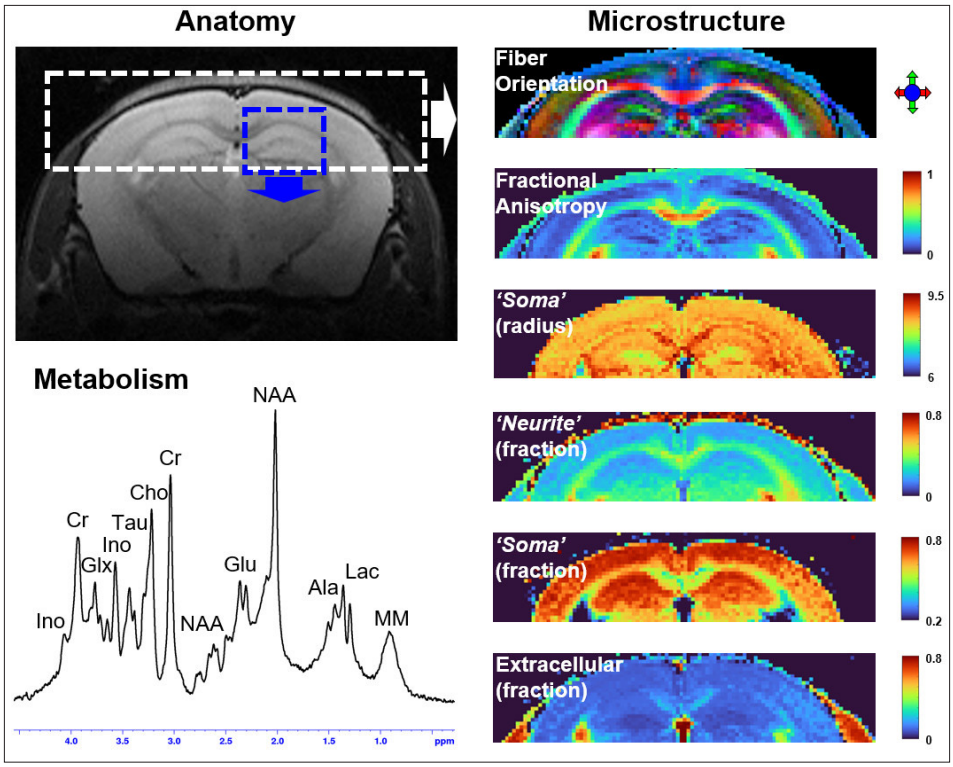

Figure 1 – Multi-parametric MRI of the mouse brain in vivo at 3 Tesla. Top-left, anatomical image (T2-RARE) corresponding to a coronal slice, with overlaid regions for microstructural and metabolic assessment (white and blue boxes, respectively). Right-side, Diffusion EPI microstructural map of the upper brain region (white box on T2-RARE), computed from (top-to-bottom): Diffusion Tensor and Kurtosis Imaging fitting (DTI-DKI principal fiber orientation and fractional anisotropy) – col. Dr Rafael Henriques, University of Lisbon, Portugal; Multi-compartment modeling (SANDI: sphere 'soma' radius, μm; and stick 'neurite', sphere 'soma', and extracellular fractions) – col. Dr. Andrada Ianus, King's College London, UK. Bottom-left, semi-LASER localized spectroscopy, displaying the metabolic profile of a 2.5x2x2.5 mm voxel centered in the hippocampus (blue box on T2-RARE) with major peak assignments: Ala, alanine; Cho, choline compounds; Cr, total creatine; Ino, myo-inositol; Glu, glutamate; Glx, glutamine-glutamate; Lac, lactate; MM, macromolecules; NAA, N-acetyl aspartate; Tau, taurine. Proc. XIX Meeting of the Portuguese Society for Neuroscience, 2025.

Equally important is the scientific environment in which this infrastructure operates. The integration of i3S within the Porto Comprehensive Cancer Center "Raquel Seruca" and its partnership with the Academic Clinical Centre ICBAS – Santo António create a unique opportunity for bidirectional translation: clinical challenges can directly inform methodological development, while preclinical discoveries can rapidly progress towards patient-oriented studies. Such interaction is essential if quantitative MRI biomarkers are to move beyond proof-of-concept and become useful tools for diagnosis, prognosis and treatment monitoring.

Portugal now possesses an unusually complementary network of preclinical MRI centers. Coimbra has demonstrated the value of MRI for investigating fundamental mechanisms of neurological disease; the Champalimaud Foundation has established international leadership in ultra-high-field methodological innovation; and Porto adds a clinically oriented 3 Tesla system designed specifically to facilitate translation. Together, these infrastructures form a continuum extending from basic research to patient-centered imaging.

The defining challenge of the next decade will be to strengthen collaboration across institutions and disciplines. Bringing together physicists, radiologists, biologists, engineers and clinicians will be fundamental for transforming technological innovation into robust imaging biomarkers capable of improving clinical decision-making. In this respect, the greatest contribution of preclinical MRI may not be the images it produces, but the bridge it creates between discovery science and precision medicine.

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