

# MRI Contrast Agents: From pH Detection to Anisotropic Relaxivity

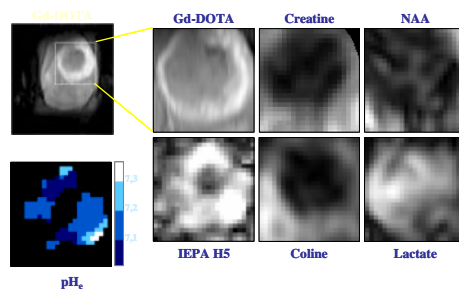
P. Ballesteros<sup>1</sup>, S. Cerdán<sup>2</sup>

<sup>1</sup>Laboratorio de Síntesis Orgánica e Imagen Molecular por Resonancia Magnética, Facultad de Ciencias, UNED, Pº Senda del Rey nº 9, 28040-Madrid, Spain

<sup>2</sup>Laboratorio de Imagen y Espectroscopía por Resonancia Magnética, Instituto de Investigaciones Biomédicas “Alberto Sols” CSIC, c/ Alberto Duperier nº 4, 28029-Madrid, Spain

Magnetic Resonance (MR) techniques are currently used routinely in the modern clinical diagnosis. Their discoverers, Professors Paul Lauterbur and Peter Mansfield were laureate in 2003 with the Nobel Prize in Physiology and Medicine. More recently, Molecular Imaging by Magnetic Resonance (MIMR) has been proposed to gain information on pathologies at the cellular and molecular level, involving a non invasive combination of MR spectroscopy and imaging techniques. In spite of the progressive sophistication of the physical MR procedures the use of Contrast Agents (CAs)<sup>1</sup> has become mandatory in many cases, fostering the development of novel diamagnetic or paramagnetic CAs to increase more sensitively and selectively the contrast of the images. The selection of the most appropriate CA in every case strongly depends on the type of diagnosis to be performed. Alterations in homeostasis of the extra-cellular environment in tissues occur very early in the disease cascade and represent a valuable target for the diagnosis of the most prevalent and morbid pathologies in developed countries, including atherosclerosis, ischemic episodes and cancer.

Our research group has contributed since long to the development of extra-cellular pH diagnosis using series of imidazolylalkanoic acid derivatives<sup>2</sup> as indicators to obtain pH maps and cerebral metabolites of implanted tumours (Figure 1) by Magnetic Resonance Spectroscopic Imaging (MRSI).



**Figure 1.** pH maps and cerebral metabolites

Beside, global pH measurements have been performed with less accuracy, using responsive paramagnetic Gd(III) CAs, CEST and PARACEST MRI techniques.<sup>3</sup> However, the isotropic relaxivity of paramagnetic CAs is not able to distinguish the directional variations in these properties. We demonstrated recently that the use of contrast agents with tubular organized nanostructures is able to distinguish directionality in the relaxation properties of tissues, opening a new avenue to image tissue anisotropy in all properties of the extra-cellular microenvironment.<sup>4</sup>

[1] Merbach A.E.; Tóth E. Eds. The chemistry of contrast agents in Medical Magnetic Resonance Imaging. Chichester: John Wiley & Sons, Ltd.; 2001.

[2] García-Martín, M. L.; Herigault, G.; Remy, C.; Flarion, F.; Ballesteros, P.; Cerdán, S.; Coles, J.; Ziegler, A. *Cancer Res.* **2001**, *61*, 6524-6531.

[3] Pérez-Mayoral, E.; Negri, V.; Soler, Jordi, Cerdán, S.; Ballesteros, P. *Eur. J. Radiol.* (2008 in press)

[4] Cerdán, S. López-Larrubia, P.; Nieto, L.; Ballesteros, P. Pérez-Mayoral, E.; P200800024.

*This work has been carried out with financial aid of CM- S-BIO/0170/2006*