

co-ordinated with the Director of the Institute / Research Unit

Research Unit Analytical Pathology (AAP)

PSP-Element:

G-500390-001

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Title of the highlight:

Spatially Resolved Quantification of Gadolinium(III)-Based Magnetic Resonance Agents in Tissue by MALDI Imaging Mass Spectrometry after In Vivo MRI

Keywords:

Imaging Agents • Imaging Mass Spectrometry • Gadolinium • MALDI • Myocardial Infarct

Central statement of the highlight in one sentence:

By precisely and quantitatively registering the histological distribution of contrast agents by MALDI Imaging Mass Spectrometry, we can make a crucial contribution to the further development and improvement of contrast agent development for MRI.

Text of the highlight:

Magnetic Resonance Imaging (MRI) offers a high-resolution procedure for the diagnostic imaging of patients. Often this procedure additionally uses contrast agents that clarify certain tissue structures and pathological processes. Gd (III)-based contrast agents improve the sensitivity and specificity of MRI, especially when targeted contrast agents are applied. Due to non-linear correlation between the contrast agent concentration in tissue and the MRI signal obtained *in vivo*, quantification of certain biological or pathophysiological processes by MRI remains a challenge. Up to now, no technology was able to provide a spatially resolved quantification of MRI agents directly within the tissue. We evaluated MALDI Imaging mass spectrometry for spatially resolved *in situ* quantification of Gd (III)-agents in correlation to *in vivo* MRI. Enhancement kinetic of Gadofluorine M was determined dynamically over time in a mouse model of myocardial infarction. MALDI Imaging was able to corroborate the *in vivo* imaging MRI signals and enabled *in situ* quantification of the gadolinium probe with high spatial resolution.

By precisely and quantitatively registering the histological distribution of those contrast agents, a crucial contribution to the further development and improvement of these substances was made.

Publication:

Aichler M, Huber K, Schilling F, Lohöfer F, Kosanke K, Meier R, Rummeny EJ, **Walch A**, Wildgruber M. Spatially Resolved Quantification of Gadolinium(III)-Based Magnetic Resonance Agents in Tissue by MALDI Imaging Mass Spectrometry after In Vivo MRI. *Angew Chem Int Ed Engl.* 2015 Feb 16.

Taking account of the HMGU mission:

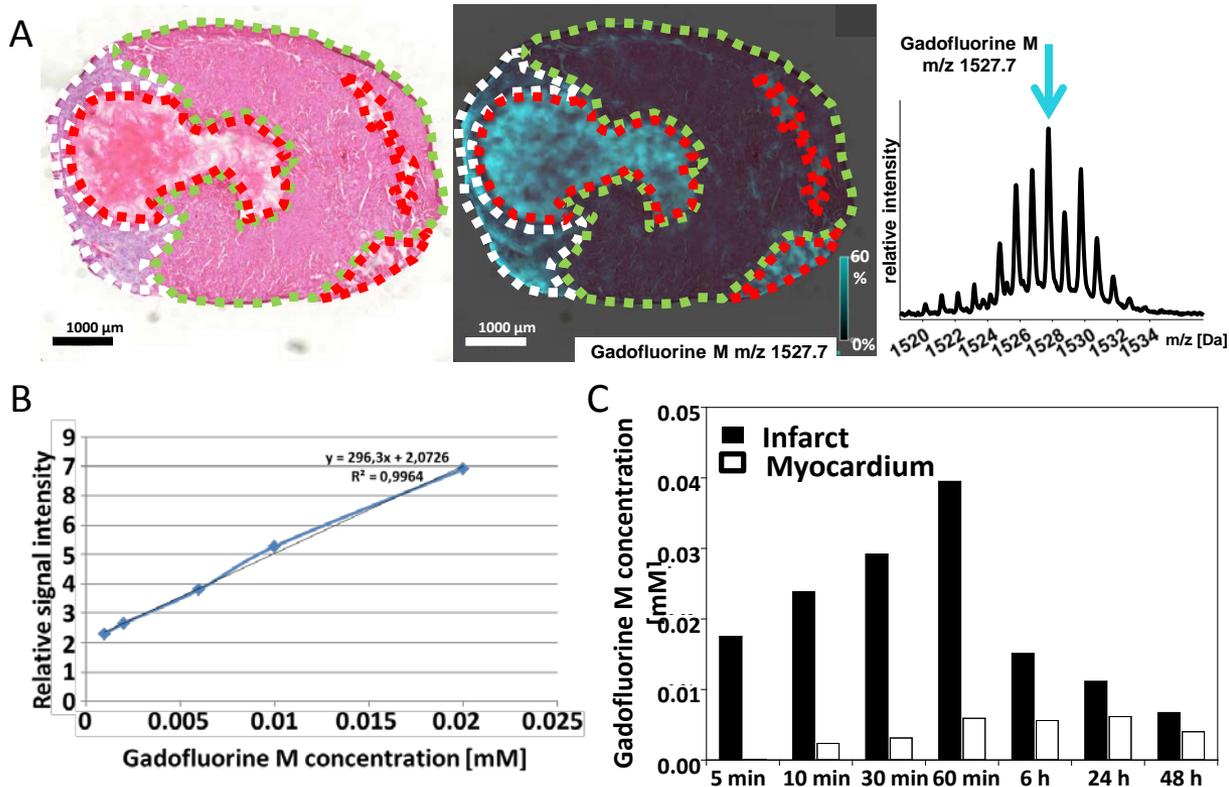
The performance of MALDI Imaging mass spectrometry provides a ground-breaking approach to molecular imaging in tissues at a microscopic level. Enabling this novel technology e.g. by the results of our study gave a new impulse for the analysis and molecular diagnostic of tissues.

The internal HMGU co-operation partners with whom the highlight was compiled, if appropriate:

NA

In vivo application of Gadofluorine M in a mouse model of myocardial infarction.

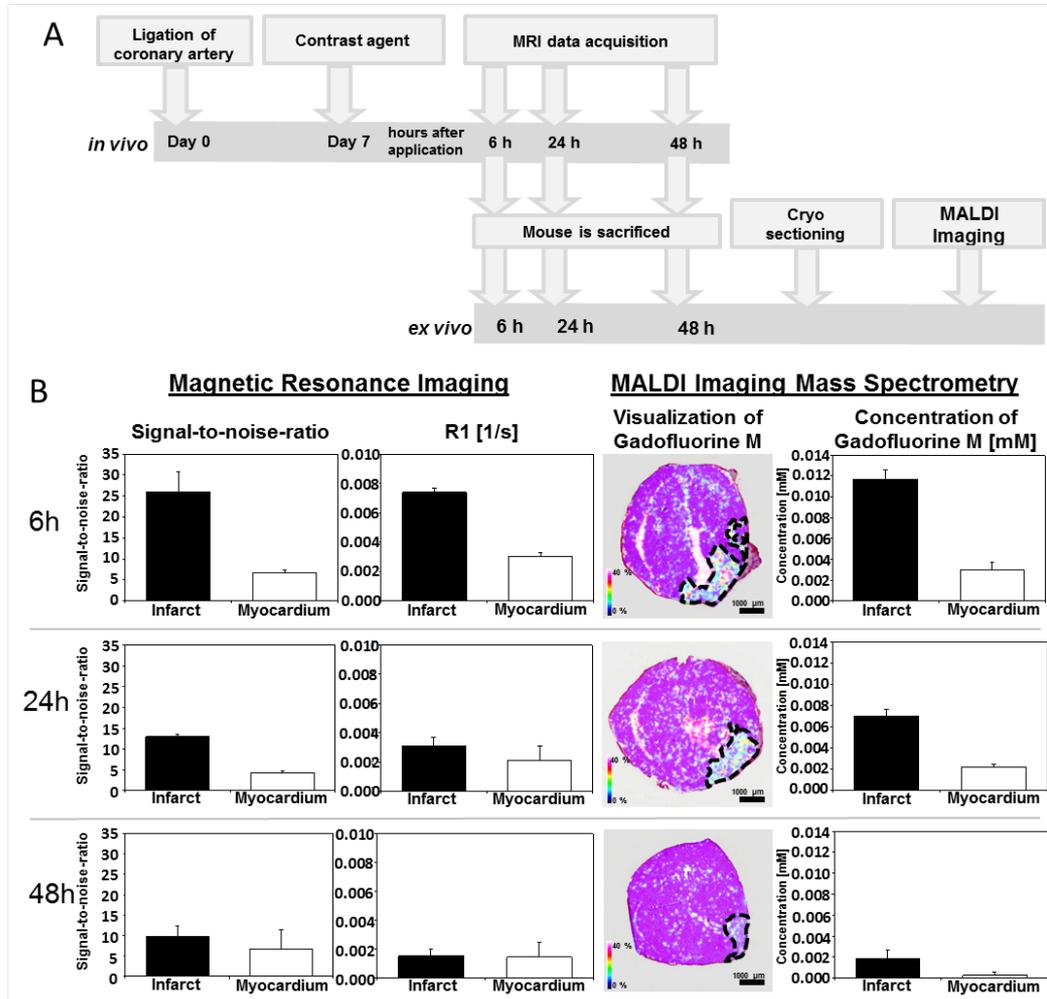
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In vivo application of Gadofluorine M in a mouse model of myocardial infarction. A) HE-stained section (left) and a MALDI imaging analysis merged with the HE-stained section (middle) are depicted. Spatially resolved Gadofluorine M concentration was detected, at 1 h post injection, showing a predominant accumulation within the infarct (white dotted line: infarcted area, green dotted line: healthy myocardium, red dotted line: blood pool). B) Standard curve for semiquantitative Gadofluorine M concentration analysis of MALDI imaging data. C) Tissue region specific kinetics of Gadofluorine M.

Correlation of MRI signals and semiquantitative MALDI imaging data of myocardial infarction after application of Gadofluorine M

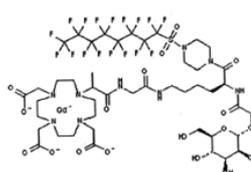
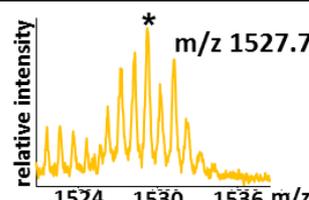
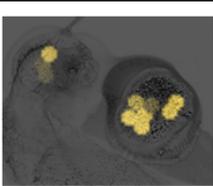
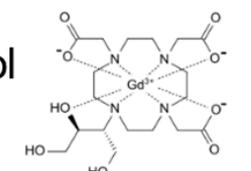
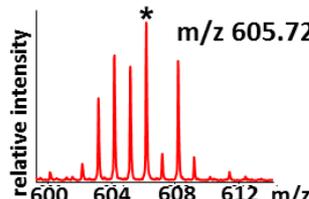
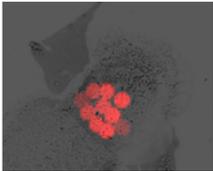
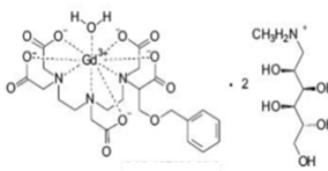
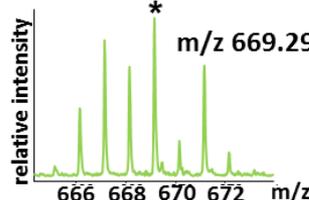
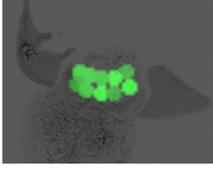
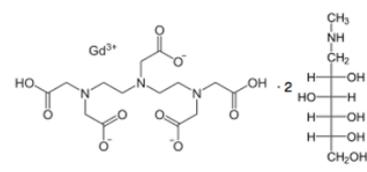
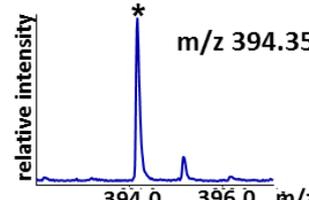
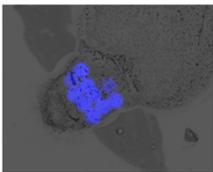
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Correlation of MRI signals and semiquantitative MALDI imaging data of myocardial infarction after application of Gadofluorine M. A) Scheme of the experimental approach. B) Direct comparison of MRI signals and MALDI imaging analysis.

Overview of analyzed gadolinium(III)-based contrast agents

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Contrast agent	Chemical structure	Mass spectrum of contrast agent	MALDI Imaging on tissue
Gadofluorine M			
Gd-DO3A-butrol (Gadovist®)			
Gd-BOTPA (Multihance®)			
Gd-DTPA (Magnevist®)			

Overview of analyzed gadolinium(III)-based contrast agents. Structural formula of analyzed compounds and resulting mass spectra of ex vivo treated tissue samples. The molecular ion signals are indicated by asterisks.