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*Review Article*

# Molecular Imaging through the Use of Mass Spectrometry and Magnetic Resonance Imaging

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**Abstract**

Sub-atomic X-ray is turning out to be progressively significant for preclinical examination. Approval of designated gadolinium tests in tissue anyway has been lumbering up to now. Therefore, a novel approach is required to evaluate the distribution of gadolinium in tissue following in vivo application. To improve the detection and quantification of Gadofluorine P deposition in scar formation and myocardial remodelling by establishing combined Magnetic Resonance Imaging and Mass Spectrometry Imaging.

**Keywords:** Molecular imaging, Gadolinium tests, Magnetic resonance, Mass spectrometry

## INTRODUCTION

The protocols for animal studies were approved by the institution. In C57BL/6J mice, permanent ligation of the left ascending artery caused myocardial infarction. At one week and six weeks after myocardial infarction, a 7T MRI was performed. Gadofluorine P was utilized for dynamic T1 planning of extracellular network blend during myocardial recuperating and contrasted with Gd-DTPA. Spatially resolved Matrix-Assisted Laser Desorption Ionization MSI and Laser Ablation-Inductively Coupled Plasma-Mass Spectrometry imaging confirmed and quantified contrast agent concentration and tissue distribution following in vivo imaging (Niemiec BA 2008).

Both Gadofluorine P improvement as well as neighbourhood tissue content in the myocardial scar was most noteworthy at 15 minutes post infusion. R1 values expanded from 1 to about a month and a half after MI resembled by an expansion in Gadofluorine P fixation in the infarct from 0.019 mM at multi week to 0.028 mM at about a month and a half, though Gd-DTPA improvement showed no distinctions. Histology affirmed expanded extracellular lattice amalgamation at 6 weeks contrasted with multi week.

The geometry, function, and biochemical adaptations of the left ventricular myocardium undergo a series of changes following ischemia. To create a stable scar from the infarct, a collagen-rich extracellular matrix is produced to replace the cardiomyocytes that have been lost. Effective infarct recuperating requires a harmony among combination and corruption of extracellular lattice to protect cardiovascular capability. Both in the infarcted and distant myocardium, excessive extracellular matrix formation can cause diastolic dysfunction by increasing wall stiffness and decreasing compliance. On the other hand, a deficiency in the production of components of the extracellular matrix can result in the progressive thinning of the myocardial wall and the expansion of the infarcted area. This raises the risk of left ventricular dilatation, which can result in either the formation of an aneurysm or even its rupture, as well as progressive heart failure (Niemiec B et al., 2020).

More precise and quantitative imaging techniques are needed to better observe ECM synthesis during myocardial remodelling and healing. Imaging of ECM remodelling is now possible thanks to the development of molecular contrast agents that bind to particular extracellular matrix proteins like collagen or elastin. Until recently, MRI was only used to make weighted, not quantitative, images **(Table 1).** The most reliable method for evaluating gadolinium-induced changes in relaxation rate is T1 mapping, which is currently the most accurate method for quantifying the accumulation of gadolinium agents. However, the local microenvironment's pH levels, oxygenation, and extra- and intracellular compartmentalization of the gadolinium

**Table 1.** General overview, and the specific characteristics and applications of MS and MRI in molecular imaging can vary depending on the specific techniques, instrumentations, and applications within the field.

| Technique | Mass Spectrometry (MS) | Magnetic Resonance Imaging (MRI) |
|---|---|---|
| Imaging Principle | Ionization and detection of mass-to-charge ratios | Detection of signals emitted by hydrogen nuclei in a magnetic field |
| Spatial Resolution | Micrometer to millimeter scale depending on the setup | Millimeter to submillimeter scale depending on the MRI machine |
| Molecular Targets | Small molecules, peptides, proteins, metabolites | Anatomical structures, tissues, organs, blood flow |
| Sensitivity | High sensitivity for detecting low-abundance molecules | Moderate sensitivity for anatomical and functional imaging |
| Quantification | Quantitative analysis of molecular species | Semi-quantitative analysis of signal intensity or contrast |
| Sample Requirements | Sample preparation, extraction, and ionization steps | Non-invasive imaging of living organisms |
| Applications | Proteomics, metabolomics, drug distribution studies | Brain imaging, cancer detection, cardiovascular imaging |
| Advantages | High specificity, molecular-level information | Non-invasive, real-time imaging of anatomical and functional changes |
| Limitations | Destructive for samples, limited depth of penetration | Relatively lower resolution compared to other imaging techniques |

molecules all have an impact on the imaging signal, which may not directly correlate with the actual amount of the molecular gadolinium probe in the tissue (Bellows J et al., 2020). Until recently, it was impossible to measure gadolinium agents in tissue with spatial resolution. After the contrast agent has been applied in vivo, Matrix Assisted Laser Desorption Ionization - Mass Spectrometry Imaging can be used to precisely visualize and quantify various gadolinium chelates in tissue sections. Quantitative resolution of gadolinium molecules in tissue can be achieved almost at cellular resolution using laser ablation, inductively coupled plasma, and mass spectrometry imaging.

In the current study, we intend to quantitatively track Gadofluorine P accumulation as a substitute for ECM concentration during myocardial healing and remodelling by combining MRI and MSI in a multiscale imaging strategy. We hypothesize that MSI provides complementary spatial and quantitative information for molecular contrast agent deposition and that Gadofluorine P would enable us to follow the process of ECM deposition in the infarct zone following experimental myocardial infarction.

# MATERIALS AND METHODS

The left anterior descending artery was permanently ligated in female C57BL/6J mice to induce myocardial infarction, as previously described. Using Gadofluorine P and Gd-DTPA as references, n = 7 mice were used for T1 mapping-based MR kinetic studies at each time point. Gd-DTPA's kinetic study took 120 minutes to complete. Due to the extended kinetic profile, an additional measurement was carried out 12 hours after Gadofluorine P administration. MR imaging was used to measure extracellular matrix synthesis over time at one week, after which mice were sacrificed, or at one and six weeks after myocardial infarction, with sample preparation for MSI and histology following (Zuluaga DJM et al., 2012). MSI-infarcted mice were sacrificed 8 minutes, 15 minutes, 21 minutes, 30 minutes, 40 minutes, and 60 minutes after the contrast agent was injected in order to evaluate the kinetics of the Gadofluorine P concentration. The local subcommittee on Research Animal Care approved all animal experiments.

# DISCUSSION

To investigate Gadofluorine P deposition during scar formation in a mouse model of myocardial infarction, we present a strategy that combines MR and MSI. We characteristic the sign increment of Gadofluorine P to post-MI scar development with expanded ECM combination and show that mice with expanded Gadofluorine P upgrade and tissue fixations have an extraordinarily superior launch division at about a month and a half post MI. According to MALDI-MSI and LA-ICP-MS, the signal increase that was detected in vivo at six weeks by MRI is accompanied by an increase in the concentration of Gadofluorine P in the tissue (Van Der CD et al., 2013).

To track the process of myocardial healing and evaluate therapy response, precise quantification of the imaging signal is essential. In vivo MRI signal quantification is still regarded as the modern MRI's Achilles' heel. SNR/CNR is not quantitative because they both depend on hardware settings and imaging parameters. T1 planning approaches permit a semi-quantitative evaluation of sign upgrade by working out the T1 an incentive for every pixel. This is semi-quantitative on the grounds that the sign saw in vivo relies upon numerous elements of the nearby climate like pH, temperature, or compartmentalization of the difference specialist. Also, designated contrast specialists alter their substance structure, sub-atomic weight and tumbling rate once bound to explicit biomarkers. As a result, it is difficult to measure the local concentration of this contrast agent in vivo because it depends on both its free and bound fractions (Unfer B et al., 2012). Techniques deciding genuine test focus in tissue post imaging would be significant to all the more likely adjudicator and further develop in vivo imaging results.

Gadofluorine M served as the basis for the development of Gadofluorine P. In a variety of animal models of atherosclerosis, it was demonstrated that Gadofluorine M binds to ECM proteins such as collagen, tenascin, and proteoglycans of the vessel wall. After a myocardial infarction, these ECM proteins can also be found in scar tissue. Due to its favourable kinetic profile, we focused on Gadofluorine P in this case. However, it should be noted that Gadofluorine P's binding constants for specific components of the extracellular matrix have not yet been reported. However, given that it is an amphiphilic agent with a structure that is similar to that of Gadofluorine M, it is expected to bind to ECM proteins and filaments due to its different surface charges. Notably, at six weeks after the MI, we found that R1 values for Gd-DTPA and Gadofluorine P varied quite a bit. This could be because of physiological variations in the healing response or because of the spatial heterogeneity of healing (Tsakos G et al., 2013).

Biphasic healing of myocardial infarction in mice has been demonstrated. Following multi week the course of myocardial renovating is currently at its start, while at the later time focuses combination of extracellular grid, development of scar tissue and rebuilding of flexible filaments has previously prompted a critical reworking of the left ventricle (Naito M et al., 2010). T1 mapping with MRI shows promise for correlating ECM deposition in the infarct zone with cardiac function during infarct healing, as evidenced by the correlation between gadofluorine P-signal intensity and tissue concentration in the infarct scar and ejection fraction six weeks later.

Only a weak correlation existed between R1 values and the concentrations of Gadofluorine P in the tissue, as determined by a direct correlation analysis. First, no pixel-by-pixel comparison was used in these correlations. This is impossible due to the fact that tissue preparation for the MALDI-MSI slides results in changes in the shape of the tissue, such as drying and shrinkage. Additionally, whereas MRI slides were 1 mm thick, MALDI-MSI slides have a thickness of 12 m. As a result, ROI-based analysis must be carried out. But more importantly, the weak point of in vivo MRI is shown by the few moderate correlations: the inability to provide sufficient quantitative data for molecular imaging. The probe's various biological and chemical surroundings have a significant impact on the signal in vivo, reducing the correlation between the measured MRI signal and the contrast agent's actual concentration (Sharda A et al., 2010). These confounders are inescapable and accentuate the need to overcome any barrier towards evaluation, which we show to be practical by MSI. Niehoff and others recently proposed to mathematically determine in vivo contrast agent concentration maps from T1 maps by calculating a conversion function from R1 and concentration values. Contrast-enhanced MRI experiments can be calibrated using spatially resolved mass spectrometry imaging thanks to the correlation between MRI and mass spectrometry imaging data.

In addition, MSI has a higher resolution than MRI: Laser ablation-inductively coupled plasma-mass spectrometry (LA-ICP-MS) can provide gadolinium distribution maps with a resolution of 15 micrometers, while MALDI-MSI currently has a resolution of 30 micrometers. This resolution, which is close to cellular levels, may make it possible to examine molecular and cellular gadolinium agents' target structures in greater depth. With the appearance of MSI, one can now match the amassing of explicit differentiation specialists spatially to their cell and atomic environmental elements (Barrieshi-Nusair K et al., 2010).

There are a few limitations to the study: 1) Accurate co-enlistment of X-ray T1 guides and gadolinium appropriation maps has not been imaginable because of the exploratory arrangement, different cut thicknesses and voxel size. 2) MALDI-MSI is a promising technology, but on the other hand, the signal is dependent on the matrix above it. However, MALDI-MSI's spatial resolution does not extend beyond the cellular range. Additionally, LA-ICP-MS is shown to be based on elemental mass spectrometry imaging, which can detect total Gd in tissue. It also provides precise, spatially resolved quantitative data and shows little matrix dependence. Additionally, LA-ICP-MS has the capability of achieving resolutions as low as 5 microns, making it an attractive alternative to MALDI-MSI. 3) For molecular MRI of cardiac tissue, gadofluorine P produces higher R1 values in the blood than in the infarct region. 4) This experimental pilot study's small sample size only permits preliminary conclusions. Particularly explores relating contrast specialist focus to flag upgrade should be acted in bigger accomplices.

# CONCLUSION

Ex vivo Mass Spectrometry Imaging can be used to validate T1 mapping, as we demonstrate. MSI makes it possible to quantify the accumulation of Gadofluorine P that is directed toward proteins in the extracellular matrix during the formation of myocardial scars. For the validation of in vivo molecular imaging and the development of future imaging biomarkers, quantitative values of gadolinium in tissue with high spatial resolution are advantageous.

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