

## MR Molecular Probes in A Clinical Setting: Potential and Issues. Early Clinical Experience

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Over the last decade, many molecular MR-imaging probes have been developed allowing for selective MR-imaging of specific targets in cancer, arteriosclerosis and inflammation, as well as providing a tool for the monitoring of therapeutic treatment. During the development of a new molecular MR imaging probe, initial proof-of-principle in-vivo imaging is typically performed in small animals (mice, rats) due to the variety of well established models available, the limited amount of agent needed and dedicated high-field animal MR-scanners. However, if the probe is designed for potential clinical use, the feasibility of such molecular MR-imaging approaches has to be translated to a large animal model with MR-imaging sequences potentially suitable for imaging in patients and established on routine clinical MR-scanners. A major hindrance toward the clinical use of molecular MR-imaging includes the amount of agent bound to the target with a sufficient SNR in the MR-image. High contrast is also necessary requiring dedicated sequence technology (depending on positive or negative contrast agents, background signal, flow etc.). In severely diseased patients, MR-scanning time is strongly limited adding further complexity. In the field of molecular cardiovascular MR-imaging motion artifacts caused by the pulse wave, flow, intrinsic cardiac and respiratory motion must be taken into account. Safety issues also present a significant concern when moving from animal models to human studies, especially if larger probe molecules (i.e. antibodies, nanoparticles) are used, due to a higher risk of allergies and longer half-life times. Thus, small molecule probes or small peptides may be of increasing interest in the future.

Finally, the complete process of probe development, pre-clinical studies and clinical trials culminating in the final approval for clinical use is time consuming and expensive. Therefore, a sufficiently large patient population and relevant clinical indication for molecular MR-imaging are needed to ensure future reimbursement.

As a consequence, most molecular MR-imaging approaches are currently limited to small animal studies while investigations in large animal models with the use of probes with high clinical impact are still rare. Only very initial studies in patients have been published to date. Many of these studies are connected to the field of arteriosclerosis and thrombosis, which are the major cause of morbidity and mortality in the western world and thus of high clinical impact.

The presentation will discuss requirements for molecular MR-imaging in large animal models and in a clinical setting, focusing on MR-imaging in the field of arteriosclerosis and thrombosis. Sequence designs with different contrast properties for clinical molecular cardiovascular MR-imaging especially in the heart, coronary arteries and carotid arteries will be addressed. Some first examples of molecular MR-imaging with translation from small animals to large animal models and finally first human studies will be presented.