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Prologue: Relevance of molecular imaging in clinical medicine

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A remarkable growth in cardiovascular imaging techniques and applications is underway. Traditionally, imaging approaches were based on anatomical and physiological assessment. In the past decade, however, the focus of imaging techniques, certainly in research, has shifted towards the visualization of physiological and pathophysiological processes at the cellular and molecular levels. Imaging at the molecular level, which can be defined as the *in vivo* characterization and measurement of biological processes, has become important, particularly in cardiovascular medicine.

Sensitive imaging techniques, including nuclear methods such as PET and single photon-emission CT, are the main molecular imaging modalities, but these techniques have low spatial resolution and lack anatomical definition. By contrast, MRI is characterized by its ability to generate three-dimensional tomographic images of opaque and soft tissue with relatively high spatial resolution. This technique can, therefore, be a useful diagnostic tool. Apart from anatomical information, metabolic and functional information can also be obtained with MRI. The degree of contrast seen on anatomical magnetic resonance images is due mainly to differences in proton density and inherent differences in the relaxation times of water in tissues. Importantly, relaxation can be manipulated with the use of exogenous contrast agents, and molecular imaging contrast agents that are MRI active have been developed by a number of research groups since the mid-1990s.

A drawback of MRI is inherent low sensitivity, and this problem has to be addressed for the technique to become a competitive molecular imaging modality. The solution might be found in the development of contrast agents with very high relaxivity levels. Progress in generating suitable agents has so far been achieved primarily through the formulation of nanoparticulate agents containing high payloads of gadolinium or iron oxide. Developments in chemistry and nanotechnology are enabling the successful synthesis of more-effective versions of these agents, making MRI an increasingly important molecular imaging technique. Importantly, multimodal MRI contrast agents have been developed that are equipped with labels for complementary imaging modalities, such as fluorescence.

Optical techniques (e.g. confocal microscopy, intravital microscopy, and fluorescence imaging) are imaging tools highly complementary to MRI. These techniques allow high-speed and high-resolution detection of multiple fluorescent species, ranging from cellular resolution at small scanning windows to whole-body imaging. The major limitation of optical methods, however, is related to the low penetration depth of light; therefore, these techniques are mostly employed *ex vivo* on excised tissues. Nevertheless, *in vivo* fluorescent techniques, such as intravital microscopy and fluorescence imaging, are becoming increasingly important. With the development of new modalities, such as near-infrared optical imaging, the penetration of optical techniques has improved from one or two millimeters to several centimeters. In addition to the aforementioned limitations, a drawback of optical techniques is the limit on the anatomical information that can be obtained. The combination of high-spatial resolution techniques, such as MRI, and optical methods would, therefore, be advantageous and can be accomplished by the design of probes that exhibit both magnetic and fluorescent properties. Nanotechnology offers the exciting possibility of creating sensitive, targeted, and macromolecular contrast agents that have multiple properties integrated.

Assembled in this supplement on cardiovascular molecular imaging is a collection of articles describing the most exciting methods and applications of molecular imaging in cardiovascular medicine. We have no doubt that this supplement will stimulate further research in this exciting field.

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Competing interests
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