Tim Leiner
Mathias Goyen
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Clinical Blood Pool MR Imaging
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With 331 Figures and 26 Tables

Springer
Clinical Blood Pool MR Imaging
The Vasovist® Product Monograph

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Magnetic resonance angiography has made great strides, with continuing improvements in hardware, pulse sequencing, and know-how allowing ever-increasing speed, resolution, and suppression of artifacts. However, an inherent physical barrier has always been limited SNR. Gadolinium contrast agents help to increase SNR by facilitating T1 relaxation, but they can be injected only at a finite rate and at a limited molar dose, and there is a rapid drop in concentration following the brief arterial phase due to redistribution into the extracellular fluid compartment. With its sixfold increase in T1 relaxivity, blood pool distribution, and longer serum half-life, Vasovist® represents a new breakthrough which promises to revolutionize MRA image quality once again.

This excellent treatise on Vasovist®, created by a team of exceptional faculty who are pioneers in MR angiography, covers the basic techniques, safety, efficacy, image processing, and pharmacoeconomic details, to successfully implement a new level of MRA image quality with this new contrast agent. In addition to improving all the usual arterial phase MRA applications, the blood pool distribution opens up new possibilities, including detecting internal bleeding and imaging stent graft endoleaks, which are reviewed in detail. In the complex, competitive field of cardiovascular imaging, this book articulates the cutting edge in imaging vascular disease.

Martin R. Prince, MD, PhD
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Almost two decades ago, Martin Prince was able to demonstrate that the limitations of non-contrast MRA techniques could be overcome by injection of contrast agent. Subsequently, contrast-enhanced-MRA established itself in clinical practice as the standard for non-invasive depiction of almost all blood vessels. MR manufacturers have addressed the demands for faster acquisition speed to allow higher resolution imaging during the finite and relatively short imaging window of first pass MRA by a combination of faster gradients, parallel imaging techniques, and novel K-space sampling strategies. However, a perceived limit for improvement in spatial resolution, coupled with the negative impact of faster acquisition on contrast-to-noise ratios, has led to the development of »Vasovist«, the first contrast agent »tailored« to the vascular tree.

With its high relaxivity and unique pharmacokinetics, Vasovist opens up new horizons in vascular diagnostics with a prolonged imaging window, enhanced topographic information, and unrivaled new visualization options. The editors and authors have made groundbreaking contributions towards establishing MR angiography in various investigative settings, rendering it more precise and applying it for diverse indications. The work presented here is founded upon the extensive experience of the editors, and it includes a broad range of experience from other scientific working groups.

This book presents the applications of Vasovist-enhanced angiography; its potential advantages, such as the change in signal-to-noise ratio and intravascular distribution, are discussed systematically, thus giving a comprehensive overview of the basic principles and imaging techniques. Presentation of the various clinical fields is well-structured and is illustrated with excellent image material that addresses the essential questions concerning vascular diagnostics. This includes imaging of the intracranial and supra-aortic vessels and visualization of the coronary arteries, as well as of the renal and visceral vessels. Key chapters cover MR angiography of the aortoiliac and peripheral vessels. Whole-body MR angiography represents a special challenge for angiography. The new options offered by Vasovist-enhanced MR angiography are also discussed. All in all, this monograph presents the ideal opportunity to gain relevant information, read either as a review or as a detailed account of the increasing scientific potential offered by this method of vascular MR diagnosis.

What can we predict for the future? Two decades following Dr. Prince’s (then) heretical thesis that contrast-agent injection was required for dramatically improved MRA, we are now equipped with a tailored vascular contrast agent. This development parallels improvements in scanner performance, satisfies a demand for higher spatial resolution, and opens up a whole new perspective on the benefit of additional information available from the steady state images as a routine part of the study.

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Foreword
Introduction

The successful introduction of extracellular gadolinium-based contrast agents for contrast-enhanced MR angiography, and their wide acceptance today, raise the question of what part an intravascular contrast agent might play in diagnostic imaging. The answer lies in the capacity of an intravascular agent to give us high-level diagnostic information from first pass arterial imaging and, at the same time, to yield additional diagnostic value by allowing delayed imaging from the same contrast injection.

Clinical experience gathered since the introduction of Vasovist® (Gadofosveset) appears to provide the answer «yes»: not only is Vasovist® useful for first pass arterial imaging, but it also provides high intravascular enhancement that lasts much longer and is significantly greater than that afforded by conventional extracellular agents. Taking advantage of this effect, one can now acquire additional high-resolution images in the steady state which lead to much better delineation of vessel pathology. Steady state imaging offers the possibility of depicting the entire vascular system without relevant extravasation of the contrast medium from the intravascular space.

The extended diagnostic window of Vasovist® makes the examination more convenient because it is less dependent upon bolus dynamics. Imaging of a Gadofosveset bolus missed in the first pass examination does not require an additional injection of contrast agent. For these reasons, Vasovist® may enable physicians to detect systemic vascular disease earlier and to optimize the evaluation of therapeutic options, including percutaneous intervention and vascular surgery. In addition, imaging of the vascular system and surrounding tissues in the delayed phase appears to promise new contrast mechanisms that may improve the detection of inflammatory or malignant changes.

In summary, Vasovist® has the potential to open new horizons in diagnostic MR angiography by increasing the spatial resolution and the robustness of MRA examinations and facilitating the examination of multiple vascular beds. Vasovist® was first approved in 2005, and we are now looking at an expanded spectrum of clinical applications that has rapidly evolved and addresses the majority of clinical questions in vascular medicine and related fields. Therefore, this monograph is subdivided into chapters on technology, followed by a detailed review of the clinical fields for MR angiography with Vasovist®. With this steady increase of applications and clinical experience it is necessary to review not only the technical feasibility and reliability of the method, but also the potential additional benefit for the patient. Therefore, aspects of patient management are also analyzed, with the aim of deriving more effective and comprehensive imaging standards.

We would like to thank all of the authors for their valuable contributions and dedicated collaboration, which made this current compilation of essential aspects of Vasovist®-enhanced MR imaging possible. Also, we gratefully acknowledge the contributions of our publisher, Springer, and Mr. Eric Henquinet for his constructive, friendly and patient collaboration.

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List of Abbreviations

2D  Two-dimensional
3D  Three-dimensional
3D FFT  3D Fast Fourier Transform
SSFP  Steady state free precession
ADC  Apparent diffusion coefficient
ALARA  As low as reasonably achievable
AngioSURF  Angiographic System for Unlimited Rolling Field-of-views
APAOD  Atherosclerotic peripheral arterial occlusive disease
ASSET  Array Spatial Sensitivity Encoding Technique
AVF  Arteriovenous fistulae
BBB  Blood-brain barrier
BOLD  Blood oxygenation level-dependent
BPCAs  Blood-pool contrast agents
CA  Contrast agents
CAD  Coronary artery disease
CE  Contrast-enhanced
CE-MRA  Contrast-enhanced magnetic resonance angiography
CENTRA  Contrast-enhanced timing robust angiography
CFA  Common femoral artery
CIS  Clinically isolated syndrome
CKD  Chronic kidney disease
CLI  Critical limb ischemia
CM  Contrast medium
CMR  Cardiovascular MR
CNR  Contrast-to-noise ratio
CNS  Central nervous system
CSF  Cerebrospinal fluid
CT  Computed tomography
CTA  Computed tomography angiography
CTEPH  Chronic thromboembolic pulmonary hypertension
CVC  Central venous catheters
cVR  Color volume rendering
d  Diameter
Da  Daltons
DCE-MRI  Dynamic contrast-enhanced MRI
DEALE  Declining Exponential Approximation of Life Expectancy
DKG-NT  Deutsche Krankenhausgesellschaft Nebenkostentarif
DOR  Diagnostic odds ratio
DSA  Digital subtraction angiography
DVT  Deep venous thrombosis
E/P  Equilibrium phase
ECCM  Extracellular contrast media
ECG  Electrocardiogram
EMEA  European Medicines Agency
EMF  Electromagnetic field
ECS  Extracellular space
EUS  Endoluminal ultrasonography
EVAR  Endovascular ultrasonography
F/P  First pass
FDA  US Food and Drug Administration
FDG  18Fluorodeoxyglucose
FFT  Fast Fourier-transformation
FLAIR  Fluid attenuated inversion recovery
FLASH  Fast low-angle shot
FMD  Fibromuscular Dysplasia
FNAC  Fine-needle aspiration cytology
FOV  Fields-of-view
GBCA  Gd-based contrast agent
GCP  Good clinical practice
Gd  Gadolinium
GI  Gastrointestinal
GRAPPA  Generalized Autocalibrating Partially Parallel Acquisitions
GRE  Gradient recalled echo
H&E  Histological examination
HIFU  High-intensity focused ultrasound
HNSCC  Head and neck squamous cell carcinoma
HSA  Human serum albumin
HTA  Health technology assessment
IA-DSA  Intra-arterial X-ray-based digital subtraction angiography
ICH-GCP  International Conference on Harmonisation on Good-Clinical-Practice
ICNRIP  International Commission on Non-ionizing Radiation Protection
IEC  International Electrotechnical Commission
iPAT  Integrated Parallel Acquisition Techniques
IVC  Inferior vena cava
IVUS  Intravascular ultrasound
KTWS  Klippel-Trenaunay-Weber syndrome
LAVA  Liver acquisition with volume acquisition
LGB  Lower GI bleeding
LITT  Laser-induced thermal therapy
LNT  Linear non-threshold
MAPCAs  Major aorto-pulmonary collateral arteries
MBF  Myocardial blood flow
MDCT  Multidetector computed tomography
MIP  Maximum intensity projection
MPR  Multiplanar reconstructions
MR  Magnetic resonance
MRA  Magnetic resonance angiography
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>MRCA</td>
<td>Magnetic resonance coronary angiography</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<td>MRV</td>
<td>Magnetic resonance venography</td>
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<tr>
<td>MS</td>
<td>Multi-slice</td>
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<tr>
<td>mSENSE</td>
<td>Modified SENSE</td>
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</tr>
<tr>
<td>MSI</td>
<td>Maximal-signal-intensity</td>
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<tr>
<td>MTT</td>
<td>Mean-transit-time</td>
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<tr>
<td>NSF</td>
<td>Nephrogenic systemic fibrosis</td>
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<td>PAD</td>
<td>Peripheral artery disease</td>
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<td>PAH</td>
<td>Pulmonary arterial hypertension</td>
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<tr>
<td>PAOD</td>
<td>Peripheral arterial obstructive disease</td>
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<tr>
<td>PAT-factor</td>
<td>Parallel acquisition technique factor</td>
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<tr>
<td>PC</td>
<td>Phase-contrast</td>
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<tr>
<td>PE</td>
<td>Pulmonary embolism</td>
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<tr>
<td>PET</td>
<td>Positron emission tomography</td>
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<tr>
<td>PR</td>
<td>Perfusion reserve</td>
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<tr>
<td>PTA</td>
<td>Percutaneous transluminal angioplasty</td>
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<tr>
<td>QALY</td>
<td>Quality-adjusted-life-year</td>
<td></td>
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<tr>
<td>RARE</td>
<td>Rapid acquisition with relaxation</td>
<td></td>
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<tr>
<td>RAS</td>
<td>Renal artery stenosis</td>
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<tr>
<td>RES</td>
<td>Reticuloendothelial system</td>
<td></td>
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<tr>
<td>RF</td>
<td>Radiofrequency</td>
<td></td>
</tr>
<tr>
<td>R-factor</td>
<td>Acceleration factor</td>
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<tr>
<td>RIME</td>
<td>Receptor-induced magnetization enhancement</td>
<td></td>
</tr>
<tr>
<td>RVT</td>
<td>Renal vein thrombosis</td>
<td></td>
</tr>
<tr>
<td>SAE</td>
<td>Serious adverse events</td>
<td></td>
</tr>
<tr>
<td>SAR</td>
<td>Severe adverse reactions</td>
<td></td>
</tr>
<tr>
<td>SENSE</td>
<td>Sensitivity encoding</td>
<td></td>
</tr>
<tr>
<td>SI</td>
<td>Signal intensity</td>
<td></td>
</tr>
<tr>
<td>SLE</td>
<td>Systemic lupus erythematosus</td>
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<tr>
<td>SLN</td>
<td>Sentinel lymph node</td>
<td></td>
</tr>
<tr>
<td>SMA</td>
<td>Superior mesenteric artery</td>
<td></td>
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<tr>
<td>SMASH</td>
<td>Simultaneous acquisition of spatial harmonics</td>
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<tr>
<td>SNR</td>
<td>Signal-to-noise ratio</td>
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<tr>
<td>SPECT</td>
<td>Single photon emission computed tomography</td>
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<tr>
<td>SPGR</td>
<td>Spoiled gradient recalled echo</td>
<td></td>
</tr>
<tr>
<td>SPIO</td>
<td>Superparamagnetic iron oxide particles</td>
<td></td>
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<tr>
<td>SR</td>
<td>Surface rendering</td>
<td></td>
</tr>
<tr>
<td>SSD</td>
<td>Surface-shaded display</td>
<td></td>
</tr>
<tr>
<td>SSFP</td>
<td>Steady state free precession</td>
<td></td>
</tr>
<tr>
<td>STD</td>
<td>Standard deviation</td>
<td></td>
</tr>
<tr>
<td>STIR</td>
<td>Short tau inversion recovery</td>
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<tr>
<td>SWI</td>
<td>Susceptibility-weighted imaging</td>
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<tr>
<td>T1-SE</td>
<td>T1-spin echo</td>
<td></td>
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<tr>
<td>T2-FSE</td>
<td>T2-fast spin echo</td>
<td></td>
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<tr>
<td>TAO</td>
<td>Thromboangiitis obliterans</td>
<td></td>
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<tr>
<td>TE</td>
<td>Echo time</td>
<td></td>
</tr>
<tr>
<td>THRIVE</td>
<td>T1-weighted high-resolution isotropic volume imaging</td>
<td></td>
</tr>
</tbody>
</table>

TIPS = Transjugular intrahepatic portosystemic shunts
TOF = Time-of-flight
TR = Repetition Time
TREAT = Time-resolved echoshared angiography technique
TTP = Time-to-peak
UGIB = Upper GI bleeding
USg-FNAC = Ultrasound-guided fine-needle aspiration cytology
USPIO = Ultrasmall super paramagnetic iron oxide
VESPA = Venous-enhanced subtracted peak arterial
VIBE = Volumetric interpolated breath-hold examination
VQ scan = Ventilation-perfusion scintigraphy
VRT = Volume rendering technique
VSOP = Very small superparamagnetic iron oxide
XRA = X-ray angiography
τm = Average time