Technical Advances in Cardiovascular Imaging
Flow: Advanced Techniques

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The intrinsic motion sensitivity of MRI, which is exploited in phase contrast (PC) MRI, can be used directly acquire and quantify blood flow[1,2]. PC-MRI can be employed to encode blood flow velocities along all dimensions and offers the possibility to acquire spatially registered information on three-directional blood flow simultaneously with the morphological data within a single examination.
In clinical routine, PC-MRI is typically accomplished using methods that resolve two spatial dimensions (2D) in individual slices and encode just the component of time-resolved velocity directed perpendicularly to the 2D plane. This approach allows measurements of forward, regurgitant and shunt flows in congenital and acquired heart disease.

A number of more advanced and promising flow MR imaging techniques have been reported, which allow a more comprehensive emulation of blood flow characteristics, e.g.

- Real time phase contrast MRI for the evaluation of flow changes on short time scales[3,4]
- Fourier or Bayesian multi-point velocity encoding to encode flow velocities as a separate dimension and assess sub-voxel velocity distributions[5-7]
- 4D flow MRI for the comprehensive analysis of complex time-resolved 3D blood flow characteristics[8-10]
- Direct encoding of the acceleration component of blood flow[11,12]

In this presentation the focus is set on the comprehensive evaluation of cardiovascular hemodynamics using 4D flow MRI. 4D flow MRI provides a non-invasive method for the qualitative and quantitative characterization of blood flow in heart and great vessels in 3D. Currently, ECG synchronized 4D flow MRI (also termed 'flow sensitive 4D MRI', 'time-resolved 3D velocity mapping', or '4D velocity mapping') can be employed to detect and visualize global and local blood flow characteristics in entire targeted vascular regions. A benefit compared to traditional 2D PC-MR imaging is related to the possibility to flexibly quantify and visualize cardiovascular blood flow as illustrated in figure 1.

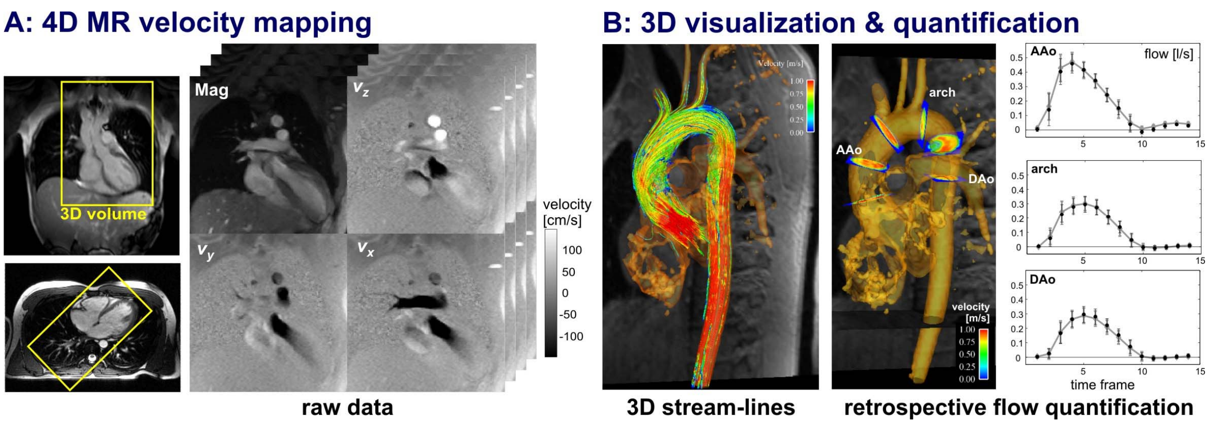

Figure 1: Acquisition of 4D flow MRI data (A) and visualization and quantification of 3D hemodynamics (B) in the aorta. The 4D velocity mapping raw data comprises information along all 3 spatial dimension, 3 velocity directions and time in the cardiac cycle. A 3D phase contrast angiogram (B, iso-surface rendering of the aorta) can be calculated from 4D flow MRI data to aid visualization and placement of analysis planes for retrospective flow quantification.

Several groups have reported advances in the application of 4D flow MRI including the analysis of blood flow through artificial valves, ventricular and atrial flow patterns, blood flow characteristics in the heart, thoracic aorta, peripheral vessels, carotid arteries, large intracranial arteries, as well as flow in the hepatic, pulmonary and venous systems[13-35].

Visualization of cardiovascular blood flow using 4D flow MRI has improved and will likely continue to improve the understanding of normal and pathologically altered cardiovascular hemodynamics. A number of studies have shown that relatively small and unsuspicious alterations in cardiac and vascular anatomy such as a mild ascending aortic aneurysms or moderate valve disease triggered surprisingly extensive alterations of local blood flow patterns. Such results indicate a potentially important role for the comprehensive analysis of hemodynamic changes based on 4D flow MRI rather than relying on simple anatomical parameters (vessel diameters, stenosis grade, etc.). However, the predictive and diagnostic value of the analyzed flow patterns and quantitative parameters are still limited. The presently available data does not (yet) allow prognostic statements and larger trials including follow-up MR examinations before and after therapy or during the progression of disease are needed to evaluate the clinical value 4D flow MRI.

A key limitation is related to the long acquisition times which may be problematic for some patients or in case of and irregular heart rate or breathing patterns. In this context, new spatio-temporal imaging acceleration techniques (k-t BLAST, k-t GRAPPA, etc.)[36-38] are promising since redundancies in two spatial encoding and the temporal dimensions can be utilized to speed up data acquisition. New methods based on the combination of phase contrast MRI and fast sampling strategies, e.g. echo-planar imaging and radial imaging with 3D PC-VIPR[15,39], have been reported and are promising for further reduction in total scan time and/or increased spatial or temporal resolution. In addition, 4D flow MRI has potential to benefit from imaging at higher field strength. Due to the small flip angles used radio frequency power deposition does not pose a major problem. The gain in signal-to-noise ratio (SNR) associated with high field CMR can be used for improved image quality and translates to reduced noise in the velocity encoded images.
In addition to long acquisition times, another limitation of 4D flow MRI is related to the complex and often time-consuming post acquisition data analysis. More automated methods for flow visualization and retrospective quantification would thus be helpful for applications within a clinical workflow. New software tools and algorithms need to be developed, for example to define standardized analysis planes in routinely acquired 4D velocity data.

In summary, 4D flow MRI has great potential for the detailed visualization of complex flow patterns associated with healthy and pathologically altered hemodynamics. The nature of such datasets (3 spatial dimensions, 3 blood flow velocity directions and time) points towards the ability of 4D flow MRI to provide detailed quantitative flow and vessel wall parameters with complete vascular coverage.

References

1. Moran PR. A flow velocity zeugmatographic interlace for NMR imaging in humans. Magnetic Resonance Imaging 1982;1:197-203.
2. Pelc NJ, Herfkens RJ, Shimakawa A, Enzmann DR. Phase contrast cine magnetic resonance imaging. Magn Reson Q 1991;7:229-54.
3. Nayak KS, Pauly JM, Kerr AB, Hu BS, Nishimura DG. Real-time color flow MRI. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2000;43:251-8.

4. Joseph AA, Merboldt KD, Voit D, Zhang S, Uecker M, Lotz J, Frahm J. Real-time phase-contrast MRI of cardiovascular blood flow using undersampled radial fast low-angle shot and nonlinear inverse reconstruction. NMR in biomedicine 2012;25:917-24.
5. Dumoulin CL, Souza SP, Hardy CJ, Ash SA. Quantitative measurement of blood flow using cylindrically localized Fourier velocity encoding. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 1991;21:242-50.
6. Macgowan CK, Kellenberger CJ, Detsky JS, Roman K, Yoo SJ. Real-time Fourier velocity encoding: an in vivo evaluation. Journal of magnetic resonance imaging : JMRI 2005;21:297-304.
7. Binter C, Knobloch V, Manka R, Sigfridsson A, Kozerke S. Bayesian multipoint velocity encoding for concurrent flow and turbulence mapping. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2013;69:1337-45.
8. Markl M, Frydrychowicz A, Kozerke S, Hope M, Wieben O. 4D flow MRI. Journal of magnetic resonance imaging : JMRI 2012;36:1015-36.
9. Markl M, Kilner PJ, Ebbers T. Comprehensive 4D velocity mapping of the heart and great vessels by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2011;13:7.
10. Wigstrom L, Sjoqvist L, Wranne B. Temporally resolved 3D phase-contrast imaging. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 1996;36:800-3.
11. Tasu JP, Jolivet O, Mousseaux E, Delouche A, Diebold B, Bittoun J. Acceleration mapping by Fourier acceleration-encoding: in vitro study and initial results in the great thoracic vessels. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 1997;38:110-6.
12. Barker AJ, Staehle F, Bock J, Jung BA, Markl M. Analysis of complex cardiovascular flow with three-component acceleration-encoded MRI. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2012;67:50-61.
13. Bachler P, Pinochet N, Sotelo J, Crelier G, Irarrazaval P, Tejos C, Uribe S. Assessment of normal flow patterns in the pulmonary circulation by using 4D magnetic resonance velocity mapping. Magn Reson Imaging 2013;31:178-88.
14. Barker AJ, Markl M, Burk J, Lorenz R, Bock J, Bauer S, Schulz-Menger J, von Knobelsdorff-Brenkenhoff F. Bicuspid aortic valve is associated with altered wall shear stress in the ascending aorta. Circ Cardiovasc Imaging 2012;5:457-66.
15. Bley TA, Johnson KM, Francois CJ, Reeder SB, Schiebler ML, B RL, Consigny D, Grist TM, Wieben O. Noninvasive assessment of transstenotic pressure gradients in porcine renal artery stenoses by using vastly undersampled phase-contrast MR angiography. Radiology 2011;261:266-73.
16. Bolger AF, Heiberg E, Karlsson M, Wigstrom L, Engvall J, Sigfridsson A, Ebbers T, Kvitting JP, Carlhall CJ, Wranne B. Transit of blood flow through the human left ventricle mapped by cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2007;9:741-7.
17. Boussel L, Rayz V, Martin A, Acevedo-Bolton G, Lawton MT, Higashida R, Smith WS, Young WL, Saloner D. Phase-contrast magnetic resonance imaging measurements in intracranial aneurysms in vivo of flow patterns, velocity fields, and wall shear stress: comparison with computational fluid dynamics. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2009;61:409-17.
18. Burk J, Blanke P, Stankovic Z, Barker A, Russe M, Geiger J, Frydrychowicz A, Langer M, Markl M. Evaluation of 3D blood flow patterns and wall shear stress in the normal and

dilated thoracic aorta using flow-sensitive 4D CMR. J Cardiovasc Magn Reson 2012;14:84.
19. Dyverfeldt P, Kvitting JP, Sigfridsson A, Engvall J, Bolger AF, Ebbers T. Assessment of fluctuating velocities in disturbed cardiovascular blood flow: in vivo feasibility of generalized phase-contrast MRI. Journal of magnetic resonance imaging : JMRI 2008;28:655-63.
20. Ebbers T, Wigstrom L, Bolger AF, Engvall J, Karlsson M. Estimation of relative cardiovascular pressures using time-resolved three-dimensional phase contrast MRI. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2001;45:872-9.
21. Francois CJ, Lum DP, Johnson KM, Landgraf BR, Bley TA, Reeder SB, Schiebler ML, Grist TM, Wieben O. Renal arteries: isotropic, high-spatial-resolution, unenhanced MR angiography with three-dimensional radial phase contrast. Radiology 2011;258:254-60.
22. Frydrychowicz A, Markl M, Hirtler D, Harloff A, Schlensak C, Geiger J, Stiller B, Arnold R. Aortic hemodynamics in patients with and without repair of aortic coarctation: in vivo analysis by 4D flow-sensitive magnetic resonance imaging. Invest Radiol 2011;46:317-25.
23. Geiger J, Markl M, Jung B, Grohmann J, Stiller B, Langer M, Arnold R. 4D-MR flow analysis in patients after repair for tetralogy of Fallot. Eur Radiol 2011;21:1651-7.
24. Harloff A, Albrecht F, Spreer J, Stalder A, Bock J, Frydrychowicz A, Schöllhorn J, Hetzel A, Schumacher M, Hennig J, Markl M. 3D blood flow characteristics in the carotid artery bifurcation assessed by flow-sensitive 4D MRI at 3T. Magnetic Resonance in Medicine 2009;61:65-74.
25. Hope MD, Hope TA, Crook SE, Ordovas KG, Urbania TH, Alley MT, Higgins CB. 4D flow CMR in assessment of valve-related ascending aortic disease. JACC Cardiovasc Imaging 2011;4:781-7.
26. Kilner PJ, Yang GZ, Wilkes AJ, Mohiaddin RH, Firmin DN, Yacoub MH. Asymmetric redirection of flow through the heart. Nature 2000;404:759-61.
27. Kvitting JP, Ebbers T, Wigstrom L, Engvall J, Olin CL, Bolger AF. Flow patterns in the aortic root and the aorta studied with time-resolved, 3-dimensional, phase-contrast magnetic resonance imaging: implications for aortic valve-sparing surgery. J Thorac Cardiovasc Surg 2004;127:1602-7.
28. Roldan-Alzate A, Frydrychowicz A, Niespodzany E, Landgraf BR, Johnson KM, Wieben O, Reeder SB. In vivo validation of 4D flow MRI for assessing the hemodynamics of portal hypertension. Journal of magnetic resonance imaging : JMRI 2013;37:1100-8.
29. Stadlbauer A, van der Riet W, Crelier G, Salomonowitz E. Accelerated time-resolved three-dimensional MR velocity mapping of blood flow patterns in the aorta using SENSE and k-t BLAST. Eur J Radiol 2010;75:e15-21.
30. Stankovic Z, Csatari Z, Deibert P, Euringer W, Blanke P, Kreisel W, Abdullah Zadeh Z, Kallfass F, Langer M, Markl M. Normal and altered three-dimensional portal venous hemodynamics in patients with liver cirrhosis. Radiology 2012;262:862-73.
31. Uribe S, Beerbaum P, Sorensen TS, Rasmusson A, Razavi R, Schaeffter T. Four-dimensional (4D) flow of the whole heart and great vessels using real-time respiratory self-gating. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2009;62:984-92.
32. Valverde I, Nordmeyer S, Uribe S, Greil G, Berger F, Kuehne T, Beerbaum P. Systemic-to-pulmonary collateral flow in patients with palliated univentricular heart physiology: measurement using cardiovascular magnetic resonance 4D velocity acquisition. J Cardiovasc Magn Reson 2012;14:25.
33. van Ooij P, Guedon A, Poelma C, Schneiders J, Rutten MC, Marquering HA, Majoie CB, Vanbavel E, Nederveen AJ. Complex flow patterns in a real-size intracranial aneurysm

phantom: phase contrast MRI compared with particle image velocimetry and computational fluid dynamics. NMR in biomedicine 2011.

34. Westenberg JJ, Roes SD, Ajmone Marsan N, Binnendijk NM, Doornbos J, Bax JJ, Reiber JH, de Roos A, van der Geest RJ. Mitral valve and tricuspid valve blood flow: accurate quantification with 3D velocity-encoded MR imaging with retrospective valve tracking. Radiology 2008;249:792-800.
35. Wetzel S, Meckel S, Frydrychowicz A, Bonati L, Radue EW, Scheffler K, Hennig J, Markl M. In vivo assessment and visualization of intracranial arterial hemodynamics with flow-sensitized 4D MR imaging at 3T. AJNR Am J Neuroradiol 2007;28:433-8.
36. Baltes C, Kozerke S, Hansen MS, Pruessmann KP, Tsao J, Boesiger P. Accelerating cine phase-contrast flow measurements using k-t BLAST and k-t SENSE. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2005;54:1430-8.
37. Carlsson M, Toger J, Kanski M, Bloch KM, Stahlberg F, Heiberg E, Arheden H. Quantification and visualization of cardiovascular 4D velocity mapping accelerated with parallel imaging or k-t BLAST: head to head comparison and validation at 1.5 T and 3 T. J Cardiovasc Magn Reson 2011;13:55.
38. Jung B, Honal M, Ullmann P, Hennig J, Markl M. Highly k-t-space-accelerated phase-contrast MRI. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2008;60:1169-77.
39. Johnson KM, Lum DP, Turski PA, Block WF, Mistretta CA, Wieben O. Improved 3D phase contrast MRI with off-resonance corrected dual echo VIPR. Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine 2008;60:1329-36.