TALK TITLE	Principles and Applications of Phase Contrast MRI
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TARGET AUDIENCE	Physicists, engineers, and research scientists interested in the physical principles, research topics, and clinical applications of phase contrast MRI.
HIGHLIGHTS	• Provide a basic and advanced understanding of PC-MRI. • Define the open research topics in PC-MRI. • Describe current and emerging clinical applications of PC-MRI.

OBJECTIVES – To define the basic physical principles of PC-MRI; provide the context for understanding the strengths and limitations of PC-MRI; and demonstrate current and emerging research and clinical applications.

INTRODUCTION – Phase contrast magnetic resonance imaging (PC-MRI) is a quantitative imaging technique that enables the non-invasive quantitative measurement of tissue velocity[1]. As such, PC-MRI can be used to measure, for example, the velocity of blood flowing throughout the cardiovascular system[2], myocardial motion during contraction[3], and cerebrospinal fluid (CSF) flow[4]. Quantitative PC-MRI flow measurements can aid clinical decision-making and help evaluate tissue function and dysfunction for both clinical and research applications.

THEORY – Whereas most of MRI evaluates the magnitude, $\left|M_{xy}e^{-i\varphi}\right|$, of the acquired complex MRI signal, PC-MRI techniques store velocity information in the phase, $\angle M_{xy}e^{-i\varphi}$, of the complex MRI signal. PC-MRI measurements require the addition of velocity encoding gradients ($\vec{g}$) to store a projection of the local velocity vector ($\vec{v}$) in the phase of the complex MRI signal such that, $\varphi(\vec{r},t) = \gamma\left(\vec{M}_0 \cdot \vec{r}(t) + \vec{M}_1 \cdot \vec{v}(t)\right) + \varphi_{off}$.

The sensitivity of the phase to velocity depends on: 1) the first moment, $M_1(t) = \gamma\int_0^t \vec{g}\,(t) \cdot \vec{r}(t)tdt$, of the gradient waveform between the peak of the RF pulse and the echo time (TE) and the spin's position history ($\vec{r}(t)$); 2) the background off-resonance phase (φ_{off})[5]; and 3) other sources of phase error (e.g. eddy currents[6], Maxwell terms[7], gradient field distortions[8], chemical shift[9], spatiotemporal undersampling[10,11]).

The user controls the velocity sensitivity by prescribing the velocity encoding strength: $VENC = \frac{\pi}{\gamma|\Delta M_1|}$ [cm/s], which should be 10-20% larger than the expected peak velocity. In order to correct for background off-resonance two measurements are typically acquired and differenced: $\Delta\varphi = \gamma\left|\Delta\vec{M}_1\right| \cdot \vec{v} = \frac{\vec{v}}{VENC}\cdot\pi$. If v exceeds the prescribed $VENC$ then the measured phase will alias because the phase interval is defined on $[-\pi, +\pi]$. Aliasing can confound the measurement. If the $VENC$ is chosen too high, then the measurement becomes less sensitive to encoding velocity and measurement inaccuracies may occur. The other sources of phase error are minimized through judicious sequence design.

In general, there are two principle ways to encode the velocity: 1) using two bi-polar flow encoding gradients ($M_{1,1} = +M_1$ and $M_{1,2} = -M_1$); or 2) using a flow compensated (FC, e.g. flow insensitive, $M_{1,1}$=0) gradient and a flow encoded (FE, $M_{1,2} = |\Delta M_1|$) gradient.

The requirement to include velocity-encoding gradients and to acquire two measurements (for off-resonance correction) extends the acquisition duration by >2-fold compared to conventional spoiled gradient echo sequences. Hence, sequence efficiency[12], acceleration methods[13,14], and the use of contrast agents[15] can improve patient acceptance by reducing exam times, but must be used judiciously so as not to impact significantly measurement precision and accuracy.

METHODS – PC-MRI data are acquired for research and clinical applications using one of several methods and each has notable advantages and disadvantages. For many applications PC-MRI experiments are synchronized to the cardiac cycle via the ECG, which enables time-resolved imaging of periodic flow events using *k*-space segmented acquisitions. Real-time PC-MRI approaches have also been demonstrated[16,17]. PC-MRI typically uses a spoiled gradient echo (SPGR), but the use of balanced steady-state free-precession has been demonstrated[18].

Two-dimensional (2D) PC-MRI – 2D PC-MRI refers to temporally resolved 2D imaging plus a single direction of velocity encoding. This is the most widespread implementation of PC-MRI. 2D PC-MRI has particular *advantage* for measuring through-plane velocity in territories for which there is a single predominant direction of flow (e.g. straight vessels). A *disadvantage* of this approach is the sensitivity to phase errors, which confound measurement accuracy.

With 2D PC-MRI it is also possible to measure all three components of the local velocity (e.g. v_x, v_y, and v_z), this requires a total of four measurements (including an off-resonance correction). An *advantage* of encoding multiple velocity components is apparent when the principle direction of flow is not known *a priori* and deviates significantly from the through-plane axis (e.g. eccentric valvular jets); a *disadvantage* is the 2-fold increase in required data compared to conventional single-direction velocity encoded 2D PC-MRI.

Four-dimensional (4D) PC-MRI - 4D PC-MRI refers to temporally resolved 3D imaging plus three directions of velocity encoding. The literature sometimes refers to this as 7D PC-MRI. 4D PC-MRI is a rapidly emerging clinical method and still an area of very active research[19]. The principle *advantages* of 4D PC-MRI lie in: 1) the exceptionally rich dataset that is amendable to multi-planar reformatting and enables the evaluation of through-plane flow or jets for any imaging plane; 2) flow visualization and analysis over larger regions of interest (e.g. four chambers of the heart or the entire thoracic aorta); and 3) no need to prospectively plan specific imaging planes during the patient's exam, but rather only select an appropriate imaging volume.

A principle *disadvantage* of 4D PC-MRI is the extended acquisition intervals due to the requirement to acquire considerable amounts of data. A 3D SPGR segmented cardiac acquisition with 2x2x2mm spatial resolution and 50ms temporal resolution acquire ~500,000+ echoes and require 45-60 minutes for image acquisition if unaccelerated. Hence, optimal sequence design, parallel imaging, compressed sensing, and non-Cartesian undersampling are essential for reducing total exam time and improving patient acceptance. Additional *disadvantages* include the somewhat limited spatiotemporal resolution due to scan time constraints and the need for sophisticated post-processing methods to measure and visualize the multi-dimensional data. Nevertheless, 4D PC-MRI is remarkably promising given its potential to provide insight to complex cardiovascular flow that cannot otherwise be obtained.

Parameter Selection – PC-MRI protocols require the careful selection of numerous sequence parameters must to ensure the acquisition of accurate data. The flip angle should be chosen relatively high (~30°) for 2D PC-MRI to take advantage of in-flow enhancement, but should be lower <15° for 4D PC-MRI applications to avoid saturating the blood signal. The receiver bandwidth should chosen to reduced perivascular fat chemical shift effects, especially at 3T (~800Hz/pixel)[20]. In general, it is judicious to minimize both TE and TR, but the use of an in-phase TE has been shown to be advantageous for minimizing chemical shift effects[20]. Spatial and temporal resolution should both be as high as possible, but are subject to breath hold (2D PC-MRI) or total acquisition time (4D PC-MRI) constraints. It has been shown that high temporal resolution should be favored when estimates of peak velocity (cm/s) are important and that high spatial resolution should be chosen when estimates of flow [mL] are needed[12].

APPLICATIONS – PC-MRI has numerous clinical and research applications, but is most widely used to measure cardiovascular blood flow and visualize complex cardiovascular flow patterns.

Fluid flow – PC-MRI is most commonly used to evaluate through-plane peak velocity and forward/regurgitant flow throughout the cardiovascular system with 2D PC-MRI protocols. 2D PC-MRI can be similarly used to evaluate CSF flow. 4D PC-MRI techniques are being used clinically to evaluate complex congenital[21], aneurysmal[22] flow patterns, hepatic flow[23], and to measure local velocity and flow.

Tissue motion – PC-MRI can be used to evaluate the velocity of the myocardium, which may be useful for the diagnosis and longitudinal evaluation of various cardiomyopathies[24].

DISCUSSION – PC-MRI is a remarkable method that enables the quantitative measurement of tissue velocity. A complete understanding of the MRI physics is critical to designing protocols and understanding measurement accuracy. 2D and 4D PC-MRI can still benefit from improvements in measurement accuracy and precision, which are likely to be achieved through further developments in sequence design, minimization of eddy current induced phase errors, and increases in spatiotemporal resolution through robust image acceleration techniques.

CONCLUSION – PC-MRI is amenable to measurements of fluid flow and tissue motion for both research and clinical applications, especially when a thorough understanding of the physics and sources of error are well understood and incorporated into protocol design.

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