Title of Session: Perfusion in the Brain, Heart & Body

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Highlights:

- Perfusion imaging is an important metric of tissue function that depends on blood flow at the microvascular level.
- Several perfusion MRI techniques are available, including dynamic contrast-enhanced, dynamic susceptibility contrast, and arterial spin labeling.
- Perfusion imaging has already proven useful in several body applications (e.g. measuring early tumor response to anti-angiogenic therapy, detection and staging of prostate cancer) and is under active investigation in multiple other clinical areas.

TALK TITLE: Body Perfusion Imaging

TARGET AUDIENCE – Research scientists, technologists, and physicians with an interest in the technical and clinical aspects of body perfusion MRI.

OUTCOME/OBJECTIVES – Learners will glean an understanding of the basic principles and specific techniques being investigated for body perfusion MRI, as well as clinical applications and limitations.

PURPOSE – **Perfusion** is the process by which blood is delivered to the capillary bed, thereby providing nutrients and oxygen to the tissue. The term is derived from the French verb "perfuser" meaning to "pour over or through."[1] Perfusion is typically expressed as ml (blood flow)/100g (tissue)/minute. Maintaining adequate tissue perfusion is key to the health of normal tissues. Under-perfusion results in tissue ischemia and, in severe cases, tissue death. Increased perfusion can be physiological or may be associated with inflammatory and neoplastic conditions. Magnetic resonance imaging is advantageous in that perfusion information can be directly correlated with anatomy, pathological tissues are highly conspicuous, and other functional techniques such as diffusion and spectroscopy can also be applied. In order to measure perfusion with MRI, a tracer is required that can be extrinsic (e.g gadolinium chelate) or intrinsic (e.g. arterial spin labeling). Using extrinsic contrast agents, perfusion MRI can be performed using dynamic contrast-enhanced (DCE) imaging with a T1-weighted pulse sequence or dynamic susceptibility contrast (DSC) imaging with a T2*-weighted pulse sequence. An alternative, less well-developed approach is the use of diffusible tracers such as hyperpolarized carbon-13 labeled compounds[2] or water labeled with deuterium or O^{17}. Each technique has particular advantages and drawbacks. For instance, arterial spin labeling avoids the need to administer a paramagnetic contrast agent, which is beneficial in patients with severely impaired renal function. It provides straightforward quantification of tissue perfusion, whereas quantification can be challenging when performing DCE with partially permeable gadolinium-based contrast agents. However, ASL has significant drawbacks as well, such as a low signal-to-noise ratio and sensitivity to misregistration artifact from patient motion. It is not

suitable for imaging tissues with very slow blood flow, where the tagged blood relaxes before reaching the capillary bed.[3]

In this presentation, we will consider examples of clinical applications of perfusion imaging in the body, as well as technical issues specific to particular clinical applications.

CLINICAL APPLICATIONS

Breast Cancer: Contrast-enhanced MRI is routinely used in high-risk patients in order to detect breast cancer, and also shows promise for tumor staging. Typical imaging protocols acquire data post-contrast at relatively long time intervals (e.g. every 90 seconds). Consequently, the degree of contrast enhancement in breast MRI is more related to tissue permeability than perfusion. Although breast MRI is highly sensitive for tumors, it offers limited specificity. Consequently, some patients undergo biopsy for lesions that subsequently turn out to be benign. Perfusion imaging has the potential to improve specificity, since tumor vessels have different properties (e.g. larger size, discontinuous vessel walls) than normal blood vessels.[4] Perfusion MRI has the potential to measure breast cancer response and to identify non-responders at an early stage. These individuals might then benefit from a different chemotherapeutic regimen. In one study, change in the transfer constant k_{trans} was the best predictor of pathologic nonresponse.[5] k_{trans} is a measure of contrast agent transport from the capillary bed into the tumor interstitium, and depends on both tumor blood flow and permeability. Non-responder tumors have a high k_{trans} due to the persistence and growth of tumor neovascularity. Conversely, responders have a decreased k_{trans} presumably due to shutdown of the immature tumor vessels caused by the anti-angiogenic effect of adjuvant chemotherapy. Perfusion MRI also has the potential to facilitate personalized therapies that are customized for particular genotypes.[6] In contrast to DCE, there is only limited experience using ASL techniques for measuring perfusion in breast tumors.[7] Further work is needed to show the reproducibility of perfusion MRI techniques and to demonstrate their utility for a variety of tumor sub-types.

Lungs: Both DCE and ASL techniques have been applied for the lungs. ASL techniques like FAIRER[8] are able to detect lung perfusion deficits due to pulmonary embolism. DCE techniques have been used to detect pulmonary embolism and evaluate various lung disorders such as pulmonary hypertension.[9] In order to avoid magnetic susceptibility artifacts that are prevalent in the lungs at air-soft tissue interfaces, perfusion imaging techniques need to use a very short echo time or fast spin-echo readout.

Abdomen and Pelvis: Perfusion MRI has shown promise in a variety of abdominal and pelvic applications, and is complementary to other functional MRI techniques like diffusion imaging. For instance, DCE techniques can quantify abnormal bowel wall perfusion in patients with Crohn's Disease.[10] Perfusion MRI can monitor the progress of anti-angiogenic therapies for tumors of the kidney, pancreas, and liver.[11] These therapeutic regimens are costly and response is not well-evaluated using standard RECIST criteria. Perfusion imaging has potential benefit in patients with cirrhosis[12], and for evaluating the aggressiveness of hepatocellular carcinoma. In the female pelvis, DCE MRI improves the staging accuracy for endometrial cancer and helps to differentiate tumor recurrence from radiation fibrosis.[13] In the prostate,

perfusion MRI can be particularly helpful for detecting cancerous nodules that may not be apparent with standard MRI techniques and improves staging accuracy.[14]

Musculoskeletal: Perfusion MRI using DCE or ASL techniques can be used to quantify muscle perfusion in patients with peripheral arterial disease.[15,16] DCE techniques have shown moderate utility for evaluating tumor biological activity[17] and may be helpful for differentiating between inflammatory and infectious synovitis.[18]

Conclusions: Perfusion MRI has already proven useful for a variety of clinical applications in the body. To date, perfusion techniques using contrast agents (DCE, DSC) appear most useful but ASL techniques show great promise.

REFERENCES

[1] http://en.wikipedia.org/wiki/Perfusion

[2] Grant AK et al. Perfusion Imaging with a Freely Diffusible Hyperpolarized Contrast Agent. Magn Reson Med . 2011 66(3): 746–755.

[3] Petersen ET, Zimine I, Ho YC, Golay X. Non-invasive measurement of perfusion: a critical review of arterial spin labelling techniques. Br J Radiol. 2006; 79(944):688–701.

[4] HuangW,Fisher PR, DulaimyK, et al. Detection of breast malignancy: diagnostic MR protocol for improved specificity. Radiology 2004;232(2):585–91.

[5] Ah-See ML, Makris A, Taylor NJ, et al. Early changes in functional dynamic magnetic resonance imaging predict for pathologic response to neoadjuvant chemotherapy in primary breast cancer. Clin Cancer Res 2008;14(20):6580–9.

[6] Loveless ME, Whisenant JG, Wilson K, et al. Coregistration of ultrasonography and magnetic resonance imaging with a preliminary investigation of the spatial colocalization of vascular endothelial growth factor receptor 2 expression and tumor perfusion in a murine tumor model. Mol Imaging 2009;8(4):187–98.

[7] Zhu DC, Buonocore MH. Breast tissue differentiation using arterial spin tagging. Magn Reson Med 2003;50(5):966–75.

[8] Mai VM et al. Detection of regional pulmonary perfusion deficit of the occluded lung using arterial spin labeling in magnetic resonance imaging. J Magn Reson Imaging 2000;11:97–102.

[9] Ohno Y et al. Primary Pulmonary Hypertension: 3D Dynamic Perfusion MRI for Quantitative Analysis of Regional Pulmonary Perfusion. AJR 2007; 188:48–56

[10] Maccioni F et al. New frontiers of MRI in Crohn's disease: motility imaging, diffusion-weighted imaging, perfusion MRI, MR spectroscopy, molecular imaging, and hybrid imaging (PET/MRI). Abdom Imaging (2012) 37:974–982.

[11] Haider MA et al. Hepatic Perfusion Imaging: Concepts and Application. Magn Reson Imaging Clin N Am 18 (2010) 465–475.

[12] Hagiwara M, Rusinek H, Lee VS, et al. Advanced liver fibrosis: diagnosis with 3D whole-liver perfusion MR imaging - initial experience. Radiology 2008;246(3):926-34.

[13] Sala E et al. The role of dynamic contrast-enhanced and diffusion weighted magnetic resonance imaging in the female pelvis. European Journal of Radiology 76 (2010) 367–385.

[14] Choi YJ et al. Functional MR imaging of prostate cancer. RadioGraphics 2007; 27:63–77.

[15] Wu W-C, Mohler E, Ratcliffe SJ, Wehrli FW, Detre JA, Floyd TF. Skeletal muscle microvascular flow in progressive peripheral arterial disease: assessment with continuous arterial spin-labeling perfusion magnetic resonance imaging. J Am Coll Cardiol 2012;53:2372–7.
[16] Isbell DC, Epstein FH, Zhong X, et al. Calf muscle perfusion at peak exercise in peripheral arterial disease: measurement by first-pass contrast-enhanced magnetic resonance imaging. J Magn Reson Imaging 2007;25:1013–20.
[17] Barile A et al. Musculoskeletal tumours: preliminary experience with perfusion MRI. Radiol Med. 2007 Jun;112(4):550-61.
[18] Kim EY er al. Usefulness of Dynamic Contrast-Enhanced MRI in Differentiating Between Septic Arthritis and Transient Synovitis in the Hip Joint. AJR 2012; 198:428–433