Title of Session: Cardiac MRI: Function, Perfusion, & Viability
Speaker Name: Ed DiBella, edward.dibella@hsc.utah.edu
Highlights
- Impact of respiratory and cardiac motion on perfusion imaging
- Methods for handling inter-frame respiratory motion
- Future imaging improvements

Talk Title: *Real-time/Free-breathing/Ungated Perfusion*

Target audience: Researchers and clinicians concerned with respiratory and cardiac motion effects on myocardial perfusion and interested in methods for free-breathing and/or ungated imaging.

Objectives: – After this presentation, one will be able to 1) discuss three approaches to handling respiratory motion in cardiac perfusion including estimating motion within the reconstruction, and 2) discuss potential benefits and challenges of some of the new ungated approaches.

PURPOSE: – To review a variety of methods for handling motion in myocardial perfusion MRI, and to present new methods for ungated free-breathing perfusion imaging.

METHODS & RESULTS:
Respiratory motion
While breath-hold scans are ideal in that the only changes over time are due to gadolinium concentration changes, large breaths at inopportune times can be a serious drawback. Typically, not all subjects can hold their breath long enough for the first pass study. This is especially true during pharmacological stress, or (even more challenging) at exercise stress [1, 2]. Thus respiratory motion needs to be considered.

Free-breathing perfusion scans have been shown to have good sensitivity and specificity – this is likely because physicians reading the scans are good at ignoring inter-frame motion. Intra-frame motion is generally not an issue from respiration since most acquisitions are short (<150 msec) relative to respiratory changes. Out-of-plane motion can be a consideration but is typically relatively small in free-breathing scans. For quantification or for possibly improved reading, there are essentially three ways to handle inter-frame motion.

The first method for handling the inter-frame motion, and by far the most widely used, is to register the time frames post-acquisition. Both rigid and non-rigid motion compensation methods have been explored by numerous groups – see survey in [3], and papers such as [4-8].
The change in contrast over time complicates the registration compared to typical image registration methods, but has been addressed in several different ways. For example, mutual information [9], statistically based methods [10], iterative comparisons with a reference image [11], model-based methods [12], and independent component analysis (ICA) [13] have all been formulated to work for the time-varying contrast in the images. Some of these groups have provided data in order for others to compare alternative methods on the same datasets. For example, Wollny et al. compared methods and provided data online for others to compare in [14]. And a 2014 MICCAI STACOM workshop ran a perfusion registration challenge in which different groups compared their methods directly on common datasets (see http://www.cardiacatlas.org/web/stacom2014/moco-introduction and results at https://avan.shinyapps.io/MoCoSTACOM2014/). [15]
The large number of papers for image registration of perfusion images reflects that this is not a solved problem for some datasets, although images with high SNR and relatively small motion (shallow breathing) seem to be readily registered with a number of the published techniques.

A second approach for handling inter-frame motion is relatively new. This is to include motion compensation within the image reconstruction. In particular, for high undersampling rates and for reconstructions leveraging temporal correlations, estimating motion should provide significant gains in image quality. These gains can exist whether or not motion free images are reconstructed. Examples of such approaches applied to perfusion include [16-23]. These methods are generally very computationally intensive, though it makes intuitive sense not to decouple the image reconstruction and registration processes as heavily undersampled acquisitions become the norm.

A third approach is to handle inter-frame motion by modifying the acquisition to include prospective slice-tracking. Only a few groups have reported on this approach [2, 24, 25]. An extra navigator readout is performed for each time frame and used to adjust the position of the slice in that time frame. This approach can be particularly helpful for exercise stress studies, where breathing is deep and rapid, causing significant out-of-plane motion [2]. Obtaining a robust navigator signal can be challenging at 3T [24].

What about respiratory motion issues for 3D perfusion acquisitions? More 3D perfusion studies are being published, mostly using breath-hold acquisitions. Similar issues as with 2D arise, although the fact that each 3D set of slices has the same contrast and the same timing (cardiac phase and respiratory phase) at each heartbeat makes the problem of registration easier in principle. Through-plane motion too is different in that it is likely correctable in central slices since it essentially changes only edges of the slab, and only one slab edge would have new data.

<u>Cardiac Motion</u>
Good ECG-gating is still problematic for some studies, especially at 3T. Additionally, arrhythmias are a concern that typically result in missed beats and inefficient acquisitions. These problems do not only affect perfusion scans. For example, cine scans can have gating/rhythm issues, and thus a number of groups have developed real-time or self-gated cine studies. Similar approaches are possible for perfusion, since with current advances, very rapid readouts are possible - a block of slices can be acquired repeatedly, without any gating signals. These ungated images can then be read by physicians [26], or the frames can be retrospectively binned (“self-gated”) into systole or diastole prior to reading [26] or for quantitative analysis [27, 28]. With this type of ungated free-breathing acquisition, perfusion becomes a much simpler protocol to prescribe and run on the scanner.

Ungated approaches also naturally lead to the idea of dropping the saturation pulse and acquiring 3D acquisitions at steady state [29, 30], much like 3D tumor DCE scans are done with spoiled gradient echo (SPGR) sequences. Other alternatives such as 3D SSFP with T2/T1 contrast have been published [31]. And 2D SPGR methods with single-slice [32] and multi-slice acquisitions are beginning to be studied as well. There are trade-offs with these imaging approaches; it is not clear what approach is best but it is clear that perfusion imaging has exciting times ahead.

CONCLUSION: – Advances in myocardial perfusion imaging techniques have made motion less of an issue. Free-breathing scans and even ungated acquisitions are being performed. In the future it is likely that acquisitions will become simpler and more efficient by moving more of the complexity to the image reconstruction and registration software. Such advances will widen use of the technique, increasing clinical impact.

REFERENCES:

[1] E. L. Foster, J. W. Arnold, M. Jekic, J. A. Bender, V. Balasubramanian, *et al.*, "MR-compatible treadmill for exercise stress cardiac magnetic resonance imaging," Magn Reson Med, vol. 67, pp. 880-9, 2012.

[2] T. A. Basha, S. Roujol, K. V. Kissinger, B. Goddu, S. Berg, *et al.*, "Free-breathing cardiac MR stress perfusion with real-time slice tracking," Magn Reson Med, vol. 72, pp. 689-98, 2014.

[3] V. Gupta, H. A. Kirisli, E. A. Hendriks, R. J. van der Geest, M. van de Giessen, *et al.*, "Cardiac MR perfusion image processing techniques: a survey," Med Image Anal, vol. 16, pp. 767-85, 2012.

[4] M. B. Stegmann, H. Olafsdottir, and H. B. Larsson, "Unsupervised motion-compensation of multi-slice cardiac perfusion MRI," Med Image Anal, vol. 9, pp. 394-410, 2005.

[5] H. Xue, S. Zuehlsdorff, P. Kellman, A. Arai, S. Nielles-Vallespin, *et al.*, "Unsupervised inline analysis of cardiac perfusion MRI," Med Image Comput Comput Assist Interv, vol. 12, pp. 741-9, 2009.

[6] G. Tarroni, C. Corsi, P. F. Antkowiak, F. Veronesi, C. M. Kramer, *et al.*, "Myocardial perfusion: near-automated evaluation from contrast-enhanced MR images obtained at rest and during vasodilator stress," Radiology, vol. 265, pp. 576-83, 2012.

[7] G. Wollny, M. J. Ledesma-Carbayo, P. Kellman, and A. Santos, "Exploiting quasiperiodicity in motion correction of free-breathing myocardial perfusion MRI," IEEE Trans Med Imaging, vol. 29, pp. 1516-27, 2010.

[8] G. Mihai, Y. Ding, H. Xue, Y. C. Chung, S. Rajagopalan, *et al.*, "Non-rigid registration and KLT filter to improve SNR and CNR in GRE-EPI myocardial perfusion imaging," J Biomed Sci Eng, vol. 5, pp. 871-877, 2012.

[9] G. M. Beache, F. Khalifa, A. El-Baz, and G. Gimel'farb, "Fully automated framework for the analysis of myocardial first-pass perfusion MR images," Med Phys, vol. 41, p. 102305, 2014.

[10] C. M. Gallippi, C. M. Kramer, Y. L. Hu, D. A. Vido, N. Reichek, *et al.*, "Fully automated registration and warping of contrast-enhanced first-pass perfusion images," J Cardiovasc Magn Reson, vol. 4, pp. 459-69, 2002.

[11] L. M. Bidaut and J. P. Vallee, "Automated registration of dynamic MR images for the quantification of myocardial perfusion," J Magn Reson Imaging, vol. 13, pp. 648-55, 2001.

[12] G. Adluru, E. V. R. DiBella, and M. C. Schabel, "Model-based registration for dynamic cardiac perfusion MRI," J Magn Reson Imaging, vol. 24, pp. 1062-1070, 2006.

[13] G. Wollny, P. Kellman, A. Santos, and M. J. Ledesma-Carbayo, "Automatic motion compensation of free breathing acquired myocardial perfusion data by using independent component analysis," Med Image Anal, vol. 16, pp. 1015-28, 2012.

[14] G. Wollny and P. Kellman, "Free breathing myocardial perfusion data sets for performance analysis of motion compensation algorithms," Gigascience, vol. 3, p. 23, 2014.

[15] "Statistical Atlases and Computational Models of the Heart - Imaging and Modelling Challenges," in 5th International Workshop, STACOM 2014, Held in Conjunction with MICCAI Boston, MA, 2014. Six workshop papers in LNCS 8896, http://link.springer.com/book/10.1007%2F978-3-319-14678-2

[16] S. G. Lingala, M. Nadar, C. Chefd-Hotel, L. Zhang, and M. Jacob, "Unified reconstruction and motion estimation in cardiac perfusion MRI," in Int Soc Biomedical Imaging (ISBI), Chicago, 2011, pp. 65-68.

[17] G. Adluru and E. DiBella, "Reconstruction with diffeomorphic motion compensation for undersampled dynamic MRI," in Proc of SPIE, San Diego, CA, 2013, pp. 88581X, p.1-4.

[18] S. G. Lingala, E. DiBella, and M. Jacob, "Deformation Corrected Compressed Sensing (DC-CS): A Novel Framework for Accelerated Dynamic MRI," IEEE Trans Med Imaging, vol. 34, pp. 72-85, 2015.

[19] M. Filipovic, P. A. Vuissoz, A. Codreanu, M. Claudon, and J. Felblinger, "Motion compensated generalized reconstruction for free-breathing dynamic contrast-enhanced MRI," Magn Reson Med, vol. 65, pp. 812-22, 2011.

[20] L. Ge, A. Kino, M. Griswold, J. C. Carr, and D. Li, "Free-breathing myocardial perfusion MRI using SW-CG-HYPR and motion correction," Magn Reson Med, vol. 64, pp. 1148-54, 2010.

[21] R. Otazo, E. Candes, and D. K. Sodickson, "Low-rank plus sparse matrix decomposition for accelerated dynamic MRI with separation of background and dynamic components," Magn Reson Med, 2014.

[22] N. K. Naresh, X. Chen, R. J. Roy, P. F. Antkowiak, B. H. Annex, *et al.*, "Accelerated dual-contrast first-pass perfusion MRI of the mouse heart: Development and application to diet-induced obese mice," Magn Reson Med, epub ahead of print, 2014.

[23] X. Chen, M. Salerno, Y. Yang, and F. H. Epstein, "Motion-compensated compressed sensing for dynamic contrast-enhanced MRI using regional spatiotemporal sparsity and region tracking: block low-rank sparsity with motion-guidance (BLOSM)," Magn Reson Med, vol. 72, pp. 1028-38, 2014.

[24] H. Pedersen, S. Kelle, S. Ringgaard, B. Schnackenburg, E. Nagel, *et al.*, "Quantification of myocardial perfusion using free-breathing MRI and prospective slice tracking," Magn Reson Med, vol. 61, pp. 734-8, 2009.

[25] D. E. J. Cleppien, G. Horstick, N. Abegunewardene, S. Weber, C. E. Müller, *et al.*, "Comparison of the quantitative first pass myocardial perfusion MRI with and without prospective slice tracking: Comparison between breath-hold and free-breathing condition," Magn Reson Med, vol. 64, pp. 1461-70, 2010.

[26] A. Harrison, G. Adluru, K. Damal, A. M. Shaaban, B. Wilson, *et al.*, "Rapid ungated myocardial perfusion cardiovascular magnetic resonance: preliminary diagnostic accuracy," J Cardiovasc Magn Reson, vol. 15:26, 2013.

[27] D. Chen, B. Sharif, R. Dharmakumar, L. E. Thomson, C. N. Bairey Merz, *et al.*, "Quantification of myocardial blood flow using non-ECG-triggered MR imaging," Magn Reson Med, 2014.

[28] D. Likhite, G. Adluru, N. Hu, C. McGann, and E. V. R. DiBella, "Quantification of myocardial perfusion with self-gated cardiovascular magnetic resonance," J Cardiovasc Magn Reson, vol. 17:14, 2015.

[29] E. V. R. DiBella, L. Chen, M. C. Schabel, G. Adluru, and C. J. McGann, "Myocardial perfusion acquisition without magnetization preparation or gating.," Magn Reson Med, vol. 67, pp. 609-13, 2012.

[30] A. G. Christodoulou, T. K. Hitchens, Y. L. Wu, C. Ho, and Z. P. Liang, "Improved subspace estimation for low-rank model-based accelerated cardiac imaging," IEEE Trans Biomed Eng, vol. 61, pp. 2451-7, 2014.

[31] S. Giri, H. Xue, A. Maiseyeu, R. Kroeker, S. Rajagopalan, *et al.*, "Steady-state first-pass perfusion (SSFPP): a new approach to 3D first-pass myocardial perfusion imaging," Magn Reson Med, vol. 71, pp. 133-44, 2014.

[32] B. Sharif, R. Dharmakumar, R. Arsanjani, L. Thomson, C. N. Bairey Merz, *et al.*, "Non-ECG-gated myocardial perfusion MRI using continuous magnetization-driven radial sampling," Magn Reson Med, vol. 72, pp. 1620-8, 2014.