Specialty area: Cardiovascular course: Cardiac Function, Perfusion & Tissue

Tissue Characterization: Research Promises

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HIGHLIGHTS:

- Parametric maps may be used to detect and quantify diffuse disease processes that are either focal or global.
- The ability to detect global changes that are subtle shifts from an established "normal" baseline depends on the reproducibility of the measurement.
- Parameters such as imaging protocol or scanner adjustments that affect reproducibility must be understood and tightly controlled.
- Increased confidence in parametric maps may be gained by error maps as well as maps of off-resonance and flip angle to ensure that abnormal shifts are not due to systematic biases.
- Significant bias errors in parametric maps may result from partial volume effects at tissue boundaries between myocardium and blood or fat due to limited spatial resolution.

TARGET AUDIENCE: The course is designed for scientists who want to learn more about cardiovascular clinical applications and physicians with interest in understanding practical cardiovascular MRI methods and emerging techniques. It is anticipated that a basic knowledge of cardiovascular MRI will be needed to be able to follow all of the topics. The content of the sessions is appropriate for radiologists, cardiologists as well as basic researchers.

OBJECTIVES: Users will have a greater appreciation for the sources of error in quantification using parametric maps and how to improve their confidence in analyzing measurements.

PURPOSE: Quantitative tissue characterization has the promise for detection of subtle changes that are indicative of a disease process and for facilitating objective measurements. Quantitative measurement using parametric mapping provides a means of quantification while providing the spatial context which is desired to assess the heterogeneity of the tissue and may be important in helping resolve artifacts.

METHODS: T1-mapping is used to produce a pixel-wise representation of the longitudinal magnetization parameter T1. The most widely used method for cardiac MR is the MOLLI method based on inversion recovery (IR) introduced by Messroghli, et al. [1,2]. More recently, saturation recovery (SR) methods such as SASHA [3] have been introduced in an effort to reduce T1-measurement biases and sensitivity to protocol parameters. The use of parametric mapping to measure relaxation times (T1, T2, or T2*) all share the common goal of providing an objective means of measuring changes in relaxation times that would allow early detection and quantification of disease. Given the constraints of time this talk focuses on T1-mapping and extra-cellular volume (ECV) mapping [4] methods. However, many of the general conclusions are relevant to T2-mapping.

A number of recent studies have shown the sensitivity of T1- and ECV-mapping for detection of disease with diffuse processes involving edema and or fibrosis [5-14]. Many of these studies are population

based studies which have demonstrated a correlation between small changes in T1 or ECV with disease or outcomes. The “research promise” is translating these exciting results to the reliable diagnosis of individuals where it may impact patient management. In order to base diagnostics assessments on subtle changes in parameters, the demand for improved reproducibility and measures of confidence are much greater than for population based studies. In this context, I will explore how T1-related biases in current inversion recovery methods may depend on protocol parameters and scanner adjustments, and how these must be controlled to ensure adequate reproducibility.

Image artifacts are not new to MRI. However artifacts in parametric mapping are different in appearance and less familiar. While eliminating artifacts is an ultimate goal, learning to recognize artifacts is important to achieving the desired confidence in parametric maps. Towards this aim, a number of confidence metrics will be discussed to include (a) mapping of off-resonance variations which result from variation in B0-field, (b) mapping of flip angle variation that arise from inhomogeneity of the B1-transmit field, and (c) mapping of the parameter error (SD maps) [15] that determine the random error due to noise that affects precision. By combining tissue parametric mapping with quality maps, variations due to extraneous influences may be recognized and potentially avoided.

A significant issue in the use of parametric mapping is the simplifying assumption which considers that voxels consists of a single species with a single parameter. In reality, due to the current spatial resolution, a voxel may be comprised of a mixture such as blood and myocardium or blood and fat. In this case, the value of T1 will generally be an average and can lead to erroneous results if not recognized. This is known as the partial volume effect but in some situations such as thin wall structures is not as well appreciated or easily recognized. This is particularly true when measuring subtle shifts on the order of a few percent. Use of higher spatial resolution is fundamental to mitigating partial volume effects. Prospects for higher resolution will be discussed.

RESULTS: Examples of native T1 maps are shown in Figure 1 for a normal subject (left), subject with acute myocarditis resulting in focal T1-elevation due to edema (center), and subject with cardiac amyloidosis and diffusely elevated T1 (right). In these examples, the T1-elevation is 200-300 ms greater than normal. This large a change is very clear to detect with high confidence. However, consider the case in Figure 2 with a subtle variation in the apparent T1. In this case the map appears normal with a wide window width (left) typically used by default, but a small variation is apparent in the T1-map when displayed with a narrower window (center). The regional variation is greater than 50 ms while the SD due to noise is < 9 ms which indicates that the variation is statistically significant. The question remains: is this variation real? It is not possible to be confident that this subtle variation is real without additional measurements to rule out other “bias” variations. In this example, additional measurements were not available, therefore, this study could not confidently be assessed as abnormal.

Sensitivity to variations in off-resonance [16] and flip angle (Fig. 3) may cause a variation in apparent T1 using the MOLLI method. This can lead to regional variations in apparent T1 which are artifactual when the off-resonance or flip angle varies spatially (Fig. 4). Variations in flip angle at 1.5T can be as great as 25% across the heart, and variation in off-resonance can be 50-100Hz or greater. These lead to changes

in T1 of several percent. An example of off-resonance variation that leads to subtle variation in the T1-map is illustrated in Figure 5.

Another source of error is the partial volume that results from limited spatial resolution. This is of particular concern for small structures but is even an issue for thin walled LV myocardium. As seen in Fig. 6, as the myocardial wall is several pixels width, the partial volume effect become appreciable leading to overestimation of the native T1 due to contamination by longer blood T1. The myocardial T1 might be underestimated for contrast measurements with shorter T1 in the blood pool. Partial volume effects also arise due to myocardial fat boundaries or due to the presence of intramyocardial fat which is commonly found in replacement of scar. Fat-water separated imaging may be used to rule out intramyocardial fat.

Saturation recovery methods such as SASHA which reset the magnetization for each measurement are not influenced in the same manner as inversion recovery methods. These methods have somewhat reduced precision which is traded for improved accuracy and reduced sensitivity to parameters. The reduced parameter sensitivity lessens the dependence on off-resonance and flip angle and has the potential to improve overall confidence.

CONCLUSION: The use of parametric mapping has been demonstrated in the detection of diffuse processes in cardiac disease and has been shown to be effective in population based studies. There are challenges in translating the full potential of quantitative mapping to individual subjects as a result of artifacts and bias errors. Quality maps may be a component in assessment of parametric maps. Ongoing research to improve reliability and reduce artifacts will improve the confidence of these methods.

FIGURES:

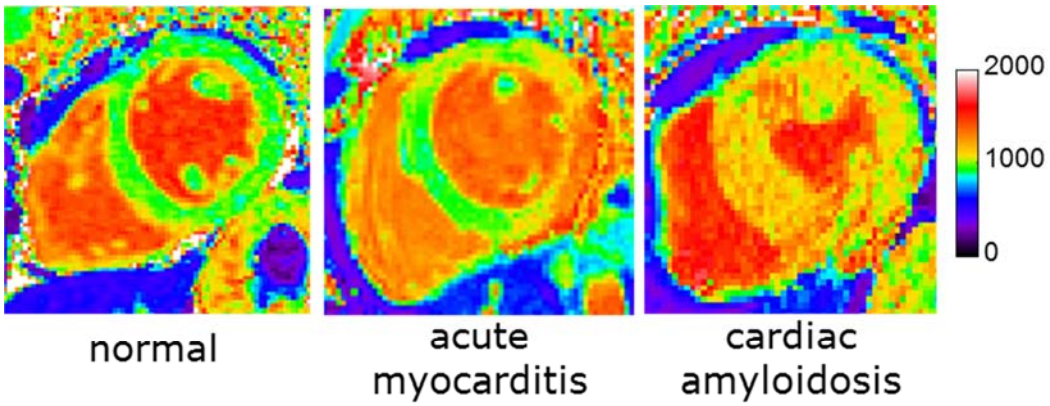

Figure 1. Native T1-maps for normal subject (left), subject with acute myocarditis resulting in focal T1-elevation due to edema (center), and subject with cardiac amyloidosis and diffusely elevated T1 (right). Elevation of native T1 with such large changes are easy to detect with high confidence.

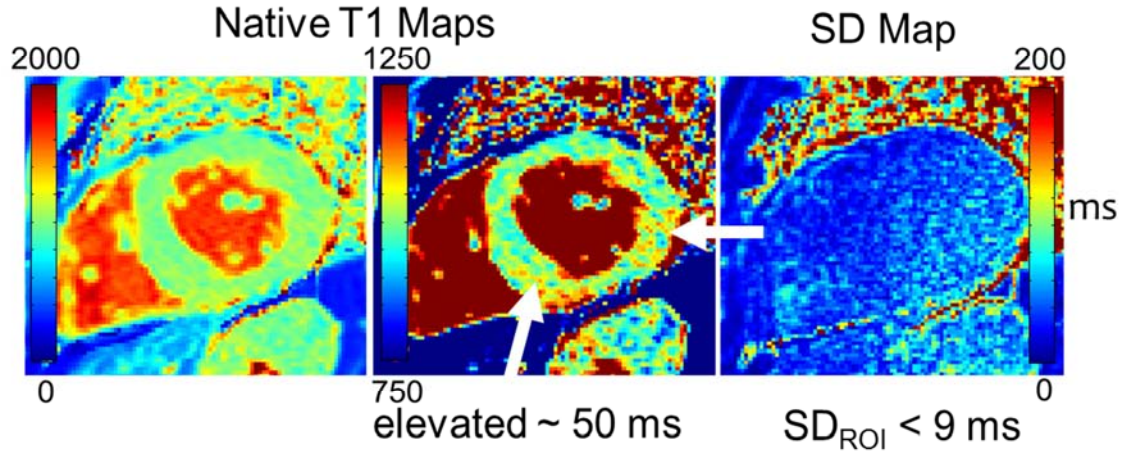

Figure. 2. Native T1-maps displayed with wide window level (left) appearing normal, and with narrower window (center) showing subtle regional variation. Regions indicated by arrows are elevated by ~50 ms. The corresponding SD in this region (SD map on right) is < 9 ms indicating the apparent elevation has statistical significance. Is the elevation real or is it artifactual due to regional variation of a systematic bias error?

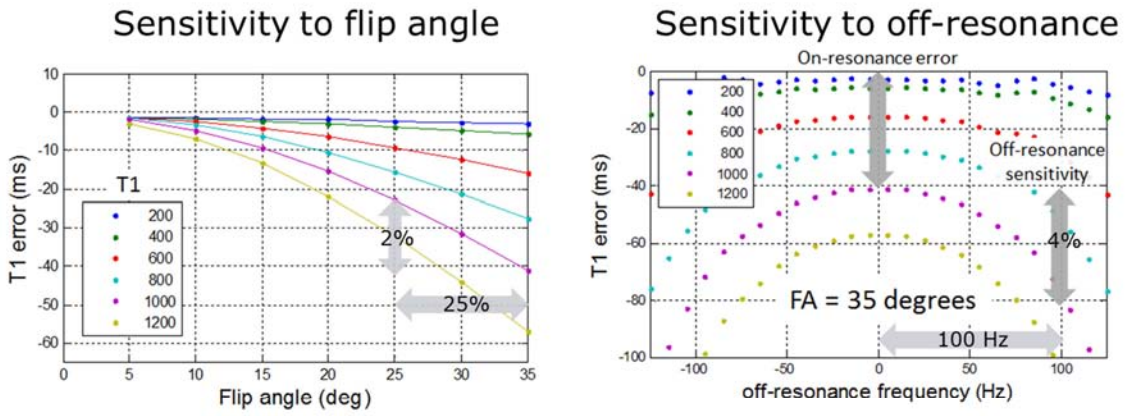

Figure 3. Sensitivity of T1 measurement using MOLLI method to variation in flip angle (left) and off-resonance (right) using a specific protocol. Spatial variation of several percent in apparent T1 may result from variations across the heart that may not be directly controlled by the user or avoided.

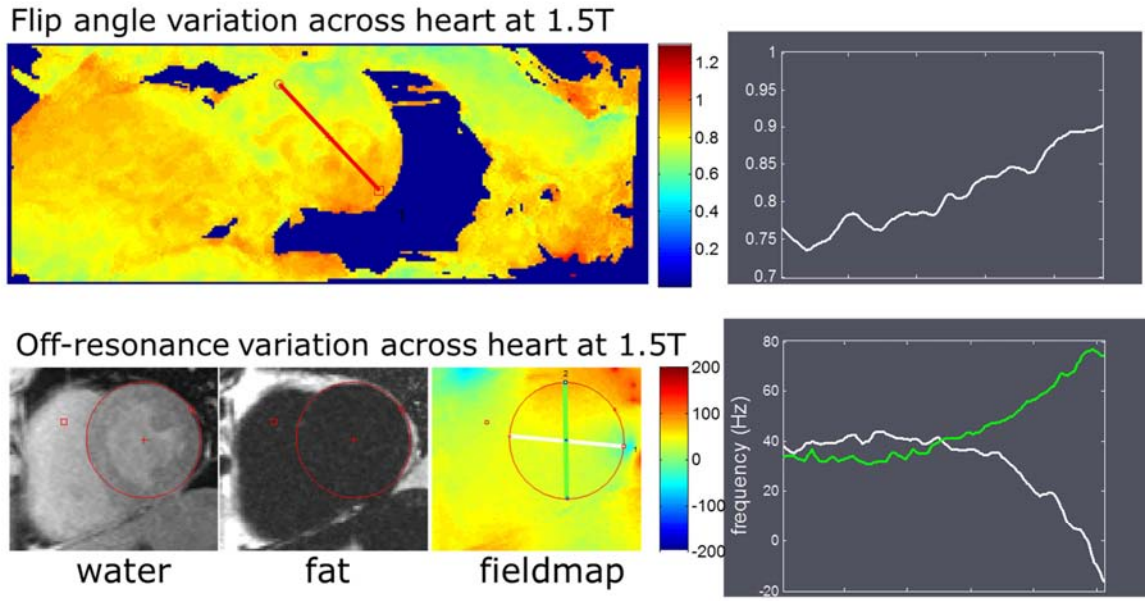

Figure. 4. Variation in flip angle across the heart (top) as measured using a saturated double flip angle method, and variation in off-resonance as measured using a multi-echo Dixon approach for fat/water separated imaging.

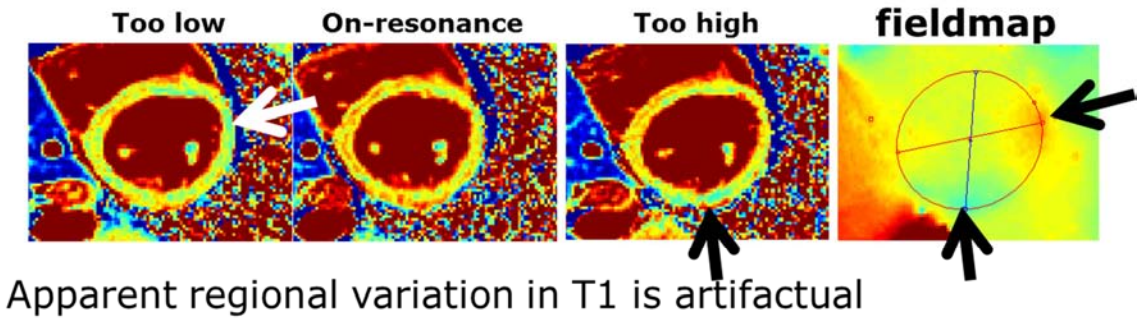

Figure 5. Variation in regional T1 due to off-resonance is artifactual.

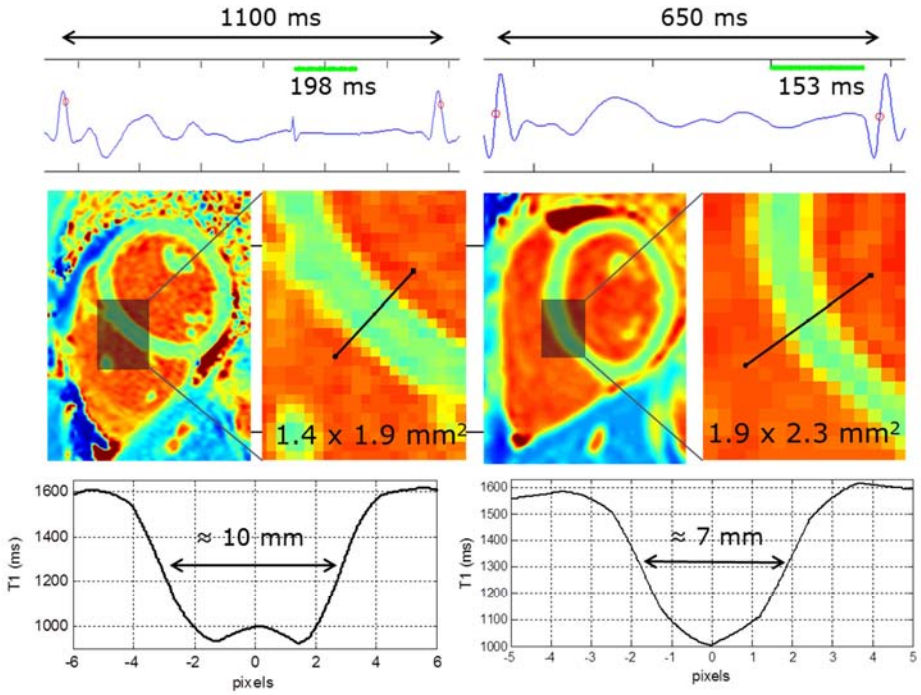

Figure. 6. Example of T1-maps in 2 subjects (a) (left) subject with heart rate of 58 bpm acquired using a MOLLI protocol with 256x144 matrix and (b) (right) subject with heart rate of approx. 90 bpm using a 192x120 matrix. Although the interpolated maps are of good quality, the subject with higher heart rate and thinner wall has only about 3.5 pixels across the septum leading to a degree of partial volume error in ROI measurements.

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