

# QIBA Musculoskeletal (MSK) Biomarker Committee (BC) Call

Tuesday, September 22, 2020 at 10 a.m. CT

## Call Summary

### In attendance

Xiaojuan Li, PhD (Co-chair)

Thomas Link, MD, PhD (Co-Chair)

Angie Botto-van Bemden, PhD

Robert Boutin, MD

John Carrino, MD, MPH

Majid Chalian, MD

Ruud de Boer, PhD

Harry Friel, MS

Maggie Fung, MEng

Ali Guermazi, MD, PhD

Youngkyoo Jung, PhD, DABR

Nancy Obuchowski, PhD

Yuxi Pang, PhD

Qi (Chris) Peng, PhD

Can Wu, PhD

### RSNA

Joe Koudelik

Susan Stanfa

**Moderator:** Dr. Link

### MSK Profile – Review Public Comments (Dr. Link)

- The Profile was released on June 26 for public comment period and the deadline has been extended to October 29
- The [MSK public comment resolution Google Sheet](#) is being used to document how feedback is addressed
- Typos and other minor errors throughout Section 3 to be corrected
- Dr. Pang recommended removing CPMG-based T2 mapping from the current profile:
  - Due to potential spin-locking effect with the CPMG T2 preparation. Reference was provided: Santyr GE, Henkelman M, Bronskill MJ. Variation in measured transverse relaxation in tissue resulting from spin locking with the CPMG sequence. J Magn Reson 79, 24-88, 1988.)
  - It may be more efficient and accurate to derive both  $T_{1\rho}$  and  $T_2$  using only one pulse sequence (MAPSS  $T_{1\rho}$ ) by varying only  $\omega_1$  in image data collection (keeping TSL constant)
- The MSK BC determined the spin-locking effect is minimal because the time interval between 180 refocusing pulses in the current MAPSS sequence (~5ms) is much longer than what was described in the paper (the authors concluded that spin-locking effect was observed when the time interval of 180 refocusing pulses  $\leq 0.25$ ms). To extrapolate  $T_2$  from  $T_{1\rho}$  dispersion by changing  $\omega_1$  is an attractive idea, which however needs further development and validation, including reproducibility evaluation.
- Recommendation to focus on best tested, best reproducibility data
- The Profile is a living document; new results and data will be incorporated into subsequent versions as available
- Current MAPSS T2 mapping uses corrected TEs, which were calculated based on the pulse width of the refocusing pulse and the assumed  $T_1/T_2$ , for T2 fitting. Dr. Pang pointed out that bias may be introduced due to T2 variation in cartilage, for example, due to magic angle effect, although  $T_1$  is relatively constant.
- The MSK BC determined a sensitivity test needs to be performed to evaluate the potential bias with variation of assumed T2
- (The sensitivity test was performed after the conference call. In the paper by Kim et al OAC 2020,  $T_1/T_2=40$  (assuming  $T_1=1.2$ s and  $T_2=30$ ms) was used. Sensitivity test was performed assuming  $T_2=60$ ms. With this doubled T2, the CV of fitted T2 btw  $T_1/T_2=40$  and  $T_1/T_2=20$  is less than 0.6%, suggesting minimal bias that will be introduced to the fitted results through assumed  $T_1/T_2$  values and corrected TEs. Data were enclosed below:

Fitting T2 (in ms)	assumed $T_1/T_2=20$	assumed $T_1/T_2=40$	CV
MFC	32.73	32.46	0.59%
MT	30.97	30.72	0.57%
LFC	23.53	23.33	0.60%
LT	25.6	25.39	0.58%
TRO	27.79	27.56	0.59%
PAT	24.5	24.3	0.58%

- Another comment related to  $T_{1\rho}$  and  $T_2$  image data interpretation as described in Section 3.8
  - Discussion re: what  $T_{1\rho}$  and  $T_2$  measure in cartilage; it was deemed necessary to advise prospective users to take magic angle effect (MAE) into account when analyzing and interpreting  $T_{1\rho}$  and  $T_2$  data.
  - The MSK BC will add according discussion in the profile.
- Discussion regarding Mr. Jonathan Clark's (EIBALL) comments
  - The Profile provides important recommendations for one of the most active areas in MSK imaging research; although it is intended for clinical practice application, there is no solid evidence regarding utility of such techniques for routine clinical care
    - It was noted that clinical utility is implemented in the Profile
- Another comment indicated that although two specific biomarkers,  $T_{1\rho}$  and  $T_2$  mapping (both deemed reasonable choices based on the current literature) are proposed, sensible alternative techniques for compositional cartilage MRI are available (e.g. GagCEST, sodium MRI, dGEMRIC, and few others) with active research underway using each of these methods
  - It was pointed out that these newer techniques are less tested, and less reproducibility data are available
  - Also, special coils required may not be available to many institutions; it is important that the Profile be able to be more widely implemented
  - The commenter proposed a more balanced introduction with an overview of available techniques; Dr. Link to update the Profile text
- In the profile a very specific pulse sequence (MAPSS), currently a research sequence, was proposed for  $T_{1\rho}$  and  $T_2$  mapping
  - The commenter noted it is somewhat concerning that the sequence is currently not generally available to researchers world-wide
  - Contact details for Siemens, GE and Philips have been added to the Profile for requesting sequence access
- Drs. Li and Link to confer re: additional contacts for soliciting public comments, e.g. ISMRM MSK Study Group Chair and OARSI
- The Profile can be published as [Stage 2: Consensus](#) on the [Profiles Page](#) on the QIBA Wiki once:
  - Consensus is reached on all public comments
  - Completed comment resolution sheet is submitted for posting on the [Comment Resolutions page](#)
  - Checklists are updated and Conformance Procedures established
  - Successful BC and CC votes

#### **Update on Special Report (Dr. Chalian)**

- Dr. Chalian has been drafting a paper based on the MSK Profile, to be submitted to *Radiology* as a "Special Report"
- Publication of this paper is intended to:
  - Highlight the recommendations and Claims presented in the Profile
  - Issue recommendations for vendors to help standardize cartilage compositional imaging
  - Communicate the required procedure to Profile users
- The length of the paper was reduced to 4800 words, as it had formerly exceeded the *Radiology* word limitation
- A few minor edits to be made by the end of September, then Dr. Chalian to circulate among BC members once more; submission to occur shortly thereafter

#### **Multisite/multivendor grant and phantom development (Dr. Li)**

- Dr. Li received R01 funding to perform a multi-center standardization study, which will help advance the Profile through technical and claim confirmation

- The study aims to develop and cross-validate novel acceleration MR T1 $\rho$  and T2 imaging methods on MR systems from multiple vendors, followed by feasibility evaluation in patients at risk for osteoarthritis
  - Aim 1: Develop novel acceleration techniques for fast 3D cartilage T1 $\rho$  and T2 imaging using model-based compressed sensing techniques
  - Aim 2: Develop a calibration phantom suitable for standardization of T1 $\rho$  and T2 measurements and implement acceleration techniques on MR systems of three major vendors (Siemens, GE and Philips); study design is based on evaluating intersite and intervender variation
  - Aim 3: Demonstrate the availability of the newly developed acceleration techniques to quantify cartilage degeneration longitudinally in a multi-vendor setting
- A new MSK phantom is currently being developed by Drs. Mirowski (Verellium, LLC) and Keenan (NIST)
  - The mechanical design of this prototype phantom was finalized based on MSK BC member feedback
  - Sample gels/solutions were sent out to NIST for initial measurements; reference values for T1, T1 $\rho$  and T2 will be measured. NIST has established protocol on providing reference values for T1 and T2; the T1 $\rho$  measure protocol will be developed.
  - The 20 internal vials can be replaced, and materials modified in the future to conduct other tests

#### **Educational/training initiative for T1 $\rho$ /T2 (Dr. Li)**

- Jason Kim, PhD (Arthritis Foundation) proposed that MSK BC member volunteers offer education to those who need additional experience in order to implement the MSK Profile
- While the MSK Profile provides general guidance, educational materials will give step-by-step instruction
- Remote training/workshops are currently being considered
- A MSK task force led by Drs. Li, Link and Peng will be formed for this initiative; MSK BC members experienced in educational initiatives were encouraged to volunteer
  - To volunteer or provide feedback, please contact Drs. Li ([lix6@ccf.org](mailto:lix6@ccf.org)) or Link ([thomas.link@ucsf.edu](mailto:thomas.link@ucsf.edu))

#### **OA Clinical Studies Forum Series organized by the Arthritis Foundation**

- "The Role of MRI in OA and Barriers to Implementation: Clinical Practice and Research" discussion will be led by Thomas Link, MD, PhD on Wednesday, October 14, 8:45 – 11:00 a.m. (PT)
- Speakers include: Tuhina Neogi, MD, PhD (Boston University), Frank Roemer, MD (University of Erlangen-Nuremberg and Boston University)
- Panelists include: Xiaojuan Li, PhD (Cleveland Clinic), Benjamin Ma, MD (UCSF), Maggie Fung (GE Healthcare), Ruud de Boer, PhD (Philips), and Xiaodong Zhong, PhD (Siemens Healthcare)

#### **Next Steps**

- Dr. Link to update the Profile in response to comments
- Staff to distribute panel discussion information, including the link to the OACM forum series upcoming events and Oct. 14 event registration link, along with call-in details for the Oct. 27 MSK BC meeting

**Next Call:** Tuesday, October 27, 2020 at 10 a.m. CT [4<sup>th</sup> Tuesdays of each month]

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