Differences in K^{trans} and v_e parameters of gluteal and deep pelvic muscles

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TARGET AUDIENCE: Radiologists; Medical physicists developing quantitative DCEMRI techniques.

PURPOSE: Dynamic contrast-enhanced MRI (DCEMRI) is increasingly used as an important tool to assess cancer therapies. DCEMRI allows application of quantitative methods that allow absolute measurement of kinetic parameters, such as K^{trans}, which can be used to assess response to therapy. Deriving the arterial input function (AIF) is crucial in determining the correct K^{trans}, but the AIF is not easily measured directly. In some pharmacokinetic modeling methods, the AIF is derived from reference tissues, typically muscle.[1] It is typically assumed that skeletal muscle is characterized by common K^{trans} and v_e values. Published values are used accordingly, including values measured in skeletal muscles, such as the calf.[2] Here, we demonstrate significant differences in values of K^{trans} and v_e between deep pelvic muscles and the gluteal muscle. We conclude that skeletal muscles should be characterized individually.

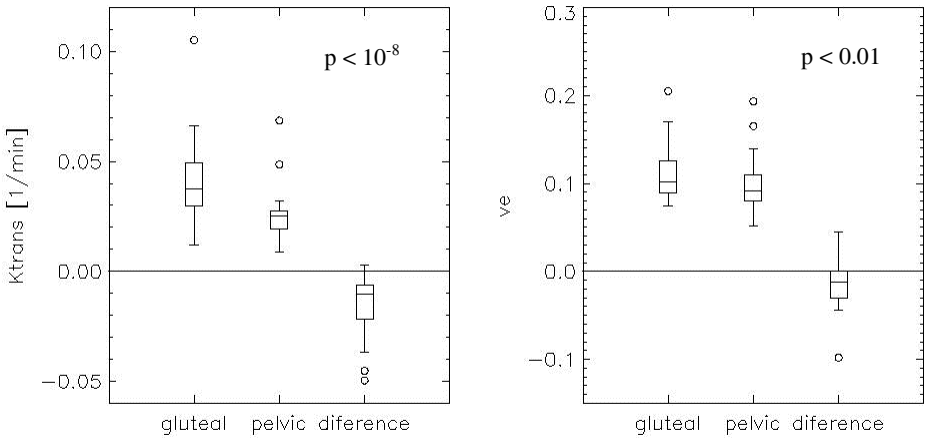

Figure 1: (LEFT) The boxplots show the distributions of K^{trans} values in gluteal and deep pelvic muscles, and the distribution of their paired differences. The p value is $< 10^{-8}$. (RIGHT) The boxplots show the distributions of v_e values in gluteal and deep pelvic muscles, and the distribution of their paired differences. The p value is < 0.01.

METHODS: In an IRB-approved and HIPAA-compliant clinical trial of a new anti-angiogenic compound (cabozantinib), male patients with castrate resistant prostate cancer were accrued after informed consent was obtained. Forty DCEMRI scans have been performed in 13 patients. The gluteal and deep pelvic muscles (psoas or obterator externus) were visible in 29 scans in 10 patients, and their K^{trans} and v_e were determined. This was achieved by acquiring a T1-weghted DCEMRI sequence, with 2 x 2 x 5 mm^3 voxels, TR/TE of 7.5/2.85 ms, flip angle of 10 degrees, and 10 s temporal resolution. All subjects received a standard dose of 0.1 mmol/kg of gadodiamide (Omniscan, GE, Waukeesha, WI), injected in under 10 s. The reference tissue method, published earlier, was used to determine the concentration of the contrast agent in the muscle.[3] K^{trans} and v_e were determined from the concentration time curves defined over regions of interest, using the Tofts model[4] and a population AIF.[5] The values of K^{trans} and v_e in the gluteal and deep pelvic muscles were compared using the non-parametric Wilcoxon signed-rank test.

RESULTS: The average values for gluteal and pelvic muscles, respectively, were 0.046 ± 0.035 min^{-1} and 0.026 ± 0.011 min^{-1} for K^{trans}, and 0.11 ± 0.03 and 0.10 ± 0.03 for v_e. We found a statistically significant change in the values of K^{trans} (by -34% on average, range -85% to +6%, $p < 10^{-8}$) and v_e (by -11% on average, range -48% to +38%, $p < 0.01$) in deep pelvic muscles, compared to the gluteal muscle. Figure 1 and 2 illustrates the values and the differences in the values of K^{trans} and v_e for the two sets of muscles.

DISCUSSION: In this work, a population AIF was used to determine K^{trans} and v_e in the muscles, and therefore the variations in the AIF due to e.g., varying cardiac output, were not accounted for, which may cause small inaccuracies in the absolute measurement of K^{trans} and v_e values. However, the goal of this work was not to provide accurate measurement of kinetic parameters, but to demonstrate significant differences between the gluteal and deep pelvic muscles. As the variations in the AIF are likely to bias both muscles' parameters in the same direction, our method of looking at paired differences is adequate, for the purpose of this work. Similarly, the effects of the anti-angiogenic drug used in the trial (cabozantinib) are likely similar for both muscles, and the validity of our paired measurements is likely not affected.

CONCLUSION: In quantitative DCEMRI experiments, the gluteal muscle is often used as the reference tissue to derive the AIF. But, this muscle is not always available in sufficient cross-section, or it may be compromised with excessive fatty infiltration, and a different muscle is used. The 34% average difference in K^{trans} between the gluteal muscle and deep pelvic muscles indicates that they need to be separately characterized for this purpose. Failure to do this may result in undue variations in K^{trans} values measured in the tumor.

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[3] Medved et al., JMRI 2004, 20(1):122-8.
[4] Tofts et al., JMRI 1999, 10(3):223-32.
[5] Parker et al., MRM 2006, 56(5):993-1000.