Metabolic imaging of \textit{in vivo} myocardium

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Background
The equilibrium cellular water efflux rate constant [k_{io}; mean water lifetime inverse] from contrast agent [CA]-enhanced MRI measures on-going cellular Na\textsuperscript{+},K\textsuperscript{+}-ATPase activity [turnover]. Good literature [4 different labs] agreement shows substantial k_{io} decreases in myocardial ischemia, hypertension, or infarct regions (Table). The 3 methods used differ in extracellular (“outside”) CA\textsubscript{o} level manipulation to change the MR shutter-speed relative to k_{io} and the MR exchange condition reached: A) CA\textsubscript{o} steady-state, slow-exchange-regime; B) CA\textsubscript{o} titration, fast-exchange-regime [FXR]; and C) CA\textsubscript{o} wash-out, FXR. The independent intracellular volume fraction [ICV] - cell density×volume product and ≈1 - ECV [extracellular volume fraction] - also decreases in pathology. We hypothesize that k_{io} mapping shows metabolic compromise most effectively. We report initial experience with tissue near a repaired ventricular septal defect [VSD].

Methods
We acquired serial 1.5T \textsuperscript{1}H\textsubscript{2}O T\textsubscript{1}-weighted data from a 27 yo male before and 3 times after a bolus IV 0.15 mmol/kg CA [Omniscan] injection. Quantitative Look-Locker T\textsubscript{1} measurements [non-selective inversion, 21 recovery times] imaged an 8 mm slice with a mid-ventricular short axis location inferior to the VSD patch. Method C (CA\textsubscript{o} wash-out, FXR) determined k_{io} and ICV values in six LV wall segments.

Results
The Figure shows a post-CA T\textsubscript{1}-w image: the endo- and epicardial LV wall edges as bright orange and green, respectively [light orange circle, an LV ROI]. Segmental ICV and k_{io} values are given (yellow). Segments S5 and S6 comprise the septum. The ICV values for segments S1 - S4 are reasonable for normal myocardium (Table). Thus, we have indicated (*) a control myocardial k_{io} value [5 s\textsuperscript{-1}, Table], since the CA wash-out data quantity [3 points] and quality from these normal myocardial segments yielded insufficient precision. Interestingly, the k_{io} value is reduced [4.5 s\textsuperscript{-1}] in segment S6, and dramatically so [1.7 s\textsuperscript{-1}; 66\%↓] in segment S5, immediately inferior to the VSD patch.

Conclusions
The k_{io} biomarker is a sensitive measure of on-going myocardial metabolic activity. Our result suggests that tissue nearby a VSD patch can be, or become, metabolically compromised.

The ultimate goal is pixel-wise k_{io} and ICV maps. [Here, nominal voxels are 2x2x8 mm\textsuperscript{3} = 32 \textmu L.] For this, one needs data with good S/N and more than 3 wash-out points. Also, method C has systematic error absent in methods A and B, which cannot be used for humans. It assumes the CA\textsubscript{o} concentration equals that of CA\textsubscript{p} [in plasma] during wash-out. This is invalid for finite CA intravasation kinetics, which may be particularly slow in myocardial lesions due to common reduced

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|}
\hline
report \ & \ method \ & \ myocardium \ & \ ICV \ & \ k_{io} (s\textsuperscript{-1}) \ \\
\hline
2006 A & ex vivo rat (perfused/.beating) & control & 5.6 & 3.7 \ \\
 & (no flow) ischemia & change & 3.8\% & 38\% \ \\
\hline
2013 B & in vivo mouse & control [n = 12] & 0.75 & 5.3 \ \\
 & chronic/hypertension [n = 17] & 0.58 & 2.3 \ \\
 & change & 136\% & 20\% \ \\
\hline
2013 C & in vivo human & control [n = 12] & 0.69 & 3.2 \ \\
 & chronic/hypertension [n = 17] & 0.55 & 2.3 \ \\
 & change & 43\% & 75\% \ \\
\hline
2014 C & in vivo human & control [n = 4] & 0.69 & 3.2 \ \\
 & chronic/hypertension [n = 20] & 0.49 & 2.5 \ \\
 & change & 43\% & 75\% \ \\
\hline
\end{tabular}
\caption{Literature reports of active trans-membrane water cycling [k_{io}] and intracellular volume fraction [ICV] values in normal and pathological myocardia.}
\end{table}
vascularization. Possible $k_{io}$ and ICV underestimations can be corrected using $K^{\text{trans}}$ [the CA extravasation transfer constant] from the bolus tissue wash-in time-course to calculate the CA intravasation rate constant.

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**Figure 2** Short axis T$_{1}$-w image slice inferior to VSD patch. The $k_{io}$ and ICV values of six LV wall segments are given. $k_{io}$ and ICV are reduced (66% and 30%, respectively) in segment S5, immediately below the patch.