Journal of Nuclear Cardiology | Official Journal of the American Society of Nuclear Cardiology

Quantification of Intramyocardial Blood Volume with ^{99m}Tc-RBC SPECT-CT Imaging – A Preclinical Study

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BACKGROUND

1 – Ischemic heart disease (IHD) has a high mortality rate [1] and can be attributed to obstructive coronary artery disease (CAD) and/or coronary microvascular disease (CMD).

2 – CMD is characterized by structural and functional impairments of the coronary microcirculation ($< 500\ \mu m$), while CAD affects the larger diameter epicardial arteries.

3 – CMD exists in a large proportion of patients with IHD and other cardiovascular diseases (i.e. hypertrophic heart disease, aortic stenosis) and may occur in individuals with and without CAD [2 – 4].

4 – Many risk factors have been proposed to contribute to CMD, such as chronic inflammation, insulin resistance, obesity, and chemotherapy and radiation therapy [5 – 8].

5 – **LVEF** has limited sensitivity [9], late manifestation [10], and large variability [11].

6 – **Concern:** No established non-invasive imaging approach to directly evaluate myocardial microcirculatory function to diagnose MVD independent of co-existing epicardial disease.

7 – **Prior Knowledge:** Microcirculation damage precedes changes in myocardial contraction and deformation (i.e. LVEF drop) [12].

8 – **Proposed Approach:** A methodological framework for absolute quantification of intramyocardial blood volume (IMBV) as a novel index of microcirculatory function with SPECT/CT imaging of ^{99m}Tc-RBCs.

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METHODS

Study Type

– Prospective preclinical imaging studies were performed under resting conditions with a dedicated cardiac hybrid SPECT/CT system.

Study Subjects

– Twelve retired female beagle breeders (weight 10.8 ± 1.0 kg) were scanned during this project. ^{99m}Tc-labeled RBCs (18.8 ± 4.3 mCi) were intravenously injected into the animal and allowed to recirculate for 15 minutes before initiation of equilibrium blood pool SPECT imaging (~10 minutes acquisition).

Study Endpoints

– Primary Endpoints:

(1) Robust estimation of IMBV *in vivo* with SPECT-CT imaging, and

(2) Validation of *in vivo* estimates of IMBV with those obtained from *ex vivo* microCT imaging following vascular casting under physiological pressures.

– Secondary Endpoint: Impact of various correction schemes on quantification of IMBV.

Study Variables

– IMBV in the end-diastolic and end-systolic phases of the cardiac cycle.

RESULTS – I

Table 1: IMBV at end-diastolic and end-systolic phases using various correction schemes. Each approach was compared (paired *t* test) to the reference fully corrected dataset (**DG + AC + SC + PVC**) presumed to be the best estimate. $P < 0.05$ was considered statistically significant.

(N = 12)	IMBV	
	End-Diastolic Phase	End-Systolic Phase
CG	0.25 ± 0.04 ($P < 0.002$)	0.21 ± 0.04 ($P < 0.002$)
CG + AC	0.25 ± 0.03 ($P < 0.002$)	0.21 ± 0.03 ($P < 0.002$)
CG + AC + SC	0.21 ± 0.03 ($P < 0.002$)	0.17 ± 0.03 ($P < 0.002$)
DG + AC + SC	0.21 ± 0.04 ($P < 0.002$)	0.17 ± 0.03 ($P < 0.002$)
DG + AC + SC + PVC	0.15 ± 0.03	0.11 ± 0.03

CG – Cardiac gating only with no other physical corrections
CG + AC – Cardiac gating with attenuation correction
CG + AC + SC – Cardiac gating with attenuation and scatter correction
DG + AC + SC – Dual cardiac and respiratory gating, attenuation and scatter correction
DG + AC + SC + PVC – Dual-gating, attenuation, scatter, and partial volume correction
IMBV – Intramyocardial blood volume
Data is represented as $\mu \pm \sigma$ $(P - value)$

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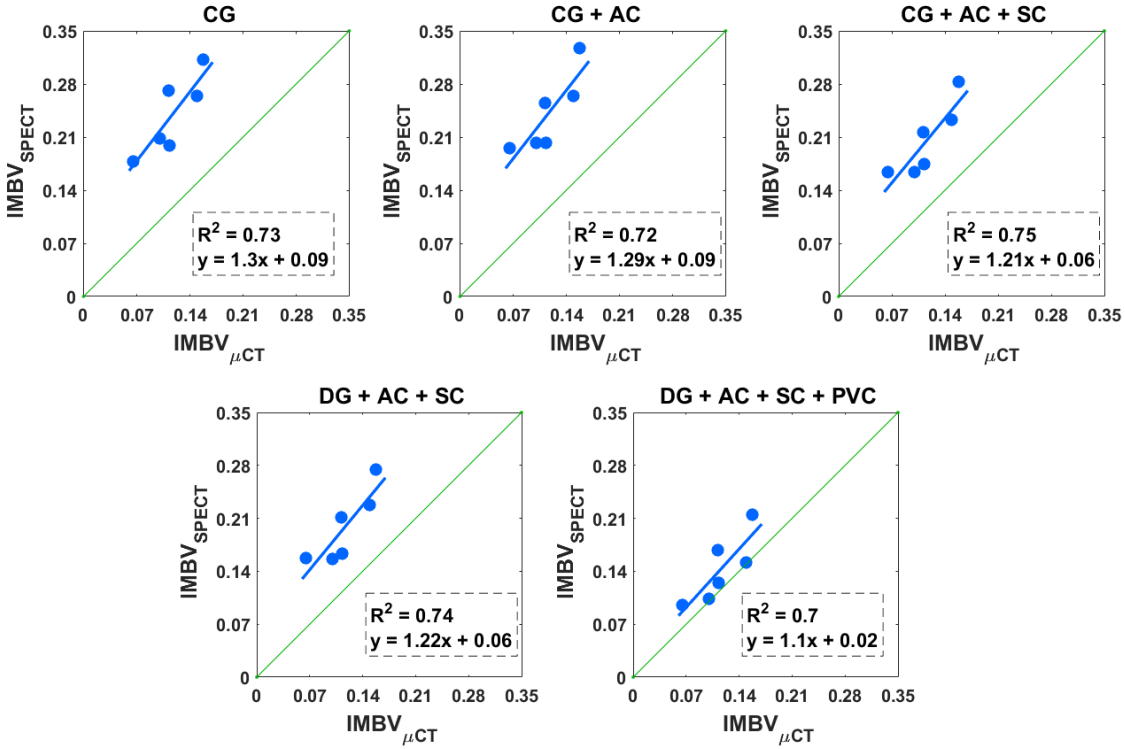
RESULTS – II

Figure 1: Correlation plots between IMBV values derived from in vivo SPECT and ex vivo microCT imaging for various correction schemes. Plots also display Pearson correlation-value squared (R^2), and the slope/intercept of linear regression fit. Green line is the line of identity. Fully corrected dataset (**DG + AC + SC + PVC**) resulted in the least overestimation (minimum bias) compared to no correction or partial correction schemes.



CONCLUSIONS

1 – **Full correction scheme** resulted in an IMBV of 0.15 ± 0.03 in the end-diastolic phase. Literature reports values in the range 0.06 – 0.20 for *in vivo* imaging studies [13 – 15] and 0.05 – 0.14 for *ex vivo* validation assays [15 – 19].

2 – Cycle-dependent changes in IMBV ($\sim 23\%$) are consistent with what is reported in the literature (i.e. $20 - 25\%$) [13, 20].

3 – Schemes that applied no correction or partial correction resulted in significant over-estimation of IMBV ($P < 0.002$).

4 – *In vivo* SPECT estimates of IMBV strongly correlated ($R^2 \geq 0.70$) with *ex vivo* measures for various correction schemes, while the **fully corrected scheme** yielded the smallest bias.

5 – While the correlations are high, SPECT derived IMBV values are generally higher than microCT derived values. This discrepancy may be caused by the resolution limit of the microCT scan (~25 μm), leading to smaller vessels being excluded from segmentation and a potential underestimation of IMBV.

6 – Accurate quantification of IMBV requires the use of anatomical information from adjunctive contrast CT imaging and corrections for cardiorespiratory motion, attenuation, scatter, and partial volume effects.

REFERENCES

[1] Association AH. Heart Disease and Stroke Statistics – At-a-Glance; 2015.
[2] Qian, J. et al., Herz 1999; 24:548-57.
[3] Fearon WF. Letter by Fearon regarding article, Circulation 2011;123:e212; author reply e3.
[4] Lanza, G.A. et al., Circulation 2010; 121:2317-25.
[5] Recio-Mayoral, A. et al., European Heart Journal 2009: ehp205.
[6] Camici, P.G. et al., The new England journal of medicine 2007; 356:830-40.
[7] Selthofer-Relatić, K. et al., Cardiology research and practice 2016; 2016.
[8] Gallucci, G. et al., Tumori 2008; 94:129-33.
[9] Ewer, M.S., et al., Journal of Clinical Oncology, 1984. 2(2): p. 112-117.
[10] Jiji, R.S., et al., Journal of Nuclear Cardiology, 2012. 19(2): p. 377-388.
[11] Galema, T.W., et al. European Heart Journal-Cardiovascular Imaging 9.2 (2008): 250-254.
[12] Daher, I.N. et al., Nature Clin. Practice Cardiovascular Medicine, 2008. 5(12): p. 797-805.
[13] Liu Y, et al., Am J Physiol-Heart C 1992; 263:H963-H7.
[14] Wu X, et al., Circulation 1992; 85:730-7.
[15] McCommis K.S., et al., Journal of the Society for CMR 2007; 9:785-92.
[16] Morgenstern C, et al., Pflügers Archiv 1973; 340:101-11.
[17] Kassab G.S., et al., Am J Physiol-Heart C 1994; 267:H2100-H13.
[18] Hoffman E, et al., Activation, metabolism and perfusion of the heart; 1987. p. 421-32.
[19] Spaan J. Circulation research 1985; 56:293-309.
[20] Pascotto M, et al., Heart 2007; 93:438-43.