Validation of Dual Energy Cardiac CT Perfusion Imaging in an Animal Model: Correlation with Coronary Flow Reserve & Fractional Flow Reserve

Background

Visual assessment of coronary lesions during invasive angiography\(^1\)\(^,\)\(^2\) or cardiac computed tomography (CT)\(^3\)\(^,\)\(^4\) correlates poorly with hemodynamic significance and often functional testing is required.

During invasive cardiac catheterisation, Coronary Flow Reserve (CFR) and Fractional Flow Reserve (FFR) can be measured using specialized guide wires. These can determine the functional significance of coronary stenoses during adenosine vasodilator stress, with CFR<2.0\(^5\) & FFR<0.80\(^1\) considered abnormal. This functional information assists in planning the need for coronary revascularisation.

Recently, it has been shown that using dual source CT myocardial perfusion defects seen at rest and with adenosine stress correlate with rest and stress defects seen on single photon emission computed tomography (SPECT) imaging\(^6\)\(^-\)\(^11\). This provides improved specificity\(^12\)\(^-\)\(^14\) to detect flow limiting coronary stenoses. Previous cardiac CT measures of perfusion have relied on assessment of the Hounsfield Unit (HU) density of the myocardium and have limited sensitivity and specificity\(^15\)\(^,\)\(^16\).

We hypothesize that quantitative assessment of the myocardium using dedicated dual energy CT acquisition\(^17\),\(^18\) and analysis\(^19\) may improve the accuracy of CT perfusion imaging. We will validate the dual energy CT perfusion measurements against invasive CFR and FFR\(^20\).

Purpose

The aim of the study is to validate the quantitative assessment of stress and rest dual energy CT myocardial perfusion imaging compared to coronary flow reserve in myocardial territories supplied by normal and stenosed coronary arteries. This data will be used to determine threshold values for normal and abnormal myocardial iodine content on rest and stress CT perfusion scans. We will also investigate the sensitivity and specificity of monoenergetic post-processing on Hounsfield unit based perfusion metrics.
**Design and Methods**

This study will aim to evaluate 10 juvenile pigs. Study animals will be prepared for surgery in the animal laboratory. The animals will be anaesthetised, intubated and mechanically ventilated. Selective coronary angiography will be performed with Judkins catheters via a femoral artery cut-down. An 0.018 inch coronary guide wire (Certus®, St Jude) will be inserted into the target artery and using a catheter exchange technique 4mm diameter methacrylate plugs (with precision drilled holes of 1-2mm diameter) will be wedged in the target artery producing a hemodynamically significant stenosis in one vascular territory. CFR and FFR measurements will be performed during an infusion of adenosine in both the stenosed artery and normal artery as the gold standard measure of myocardial blood flow in ischemic and normal myocardium.

On completion of CFR & FFR measures the pigs will be transported across the street to the Vancouver General hospital Siemens Somatom Definition Flash CT scanner.

The cardiac CT perfusion scans will be performed using standard protocol with a rest scan performed using a triphasic bolus of intravenous contrast agent. After this an adenosine infusion will be commenced and a second intravenous contrast bolus given for a stress scan.

The CT data for all scans will be transferred to a dedicated Siemens multi-modality workstation for analysis. The data is loaded into the dual energy package and analysed using the Heart Perfused Blood Volume function. This package uses proprietary software to calculate the iodine content of the myocardium and produce an iodine map.

Quantification of the myocardium on CT will be done using the syngo.via prototype software available under our master research agreement with Siemens, Germany. This software maps the contours of the endocardium and epicardium and produces a polar map using detailed pixels and the AHA 17 segment model. The software calculates the mean and standard deviation of the iodine content of the myocardium as well as the Hounsfield unit values of the endocardium and epicardium for calculation of transmural perfusion ratio (TPR). These calculations of iodine content and TPR are performed on identical myocardial segments allowing direct correlation.

The same stress and rest CT data will be also be analysed using the Monoenergetic function of the multi-modality workstation. This function models the Hounsfield unit attenuation derived if all incident photons
were a single energy. This modelled data will be saved in deciles from 40 – 140 KeV. A repeat analysis of TPR will be performed on these data sets.

**Statistical Analysis**
The data will be analysed using Student’s t-test and Z scores. Within the rest or stress studies the CT iodine concentration and TPR will be stratified in binary analysis of ischemic (defined by FFR<0.80 or CFR<2.5) Vs normal segments. The threshold value for iodine concentration and TPR on stress studies will be determined by comparing these values in normal Vs ischemic segments using receiver operator curve (ROC) analysis. The effect of Monoenergetic post-processing will be determined by comparative analysis using TPR in monoenergetic 40-140KeV datasets to determine the electron voltage for the optimal sensitivity and specificity of identifying perfusion deficits.

As this is an exploratory research question there is no published data from which to perform a power calculation. A recent abstract using a different CT perfusion technique compared FFR in 7 subjects and was able to show a difference between diseased and non-diseased vessels based on 120 segment analysis. Previous studies using animal models have shown 10 animals to be adequate to produce statistical significance using repeated measures design.

**Impact**
The CT perfusion data from this study will have direct correlation to the gold standard measure of coronary myocardial flow in normal and stenosed territories. Further correlation of the threshold values of CT iodine content and TPR with invasive FFR assessment of normal and ischemic coronary artery territories will facilitate translation of these study results to a clinical environment. The addition of validated quantified CT myocardial perfusion metrics to standard clinical cardiac CT angiography reporting may improve the accuracy of reporting difficult lesions such as those with calcification, tortuosity or motion artefact. The combination of anatomical and functional assessment in a single imaging modality could then identify lesion specific ischemia and further promote cardiac computed tomography’s role as a gate-keeper to the cardiac catheterisation laboratory for coronary revascularisation.
Appendix 1

References:


