FlowTool Method for calculating Myocardial Blood Flow

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Ammonia or Rb is injected into an arm vein. It travels to the right ventricle, is pumped to the lung, returns to the left ventricle, and then is pumped to tissues in the body including the heart muscle. Once it enters the tissue by crossing the capillary membrane, it is either irreversibly trapped or it re-crosses back into the blood stream and is removed from the tissue. A typical time series of images is shown in figure 1.

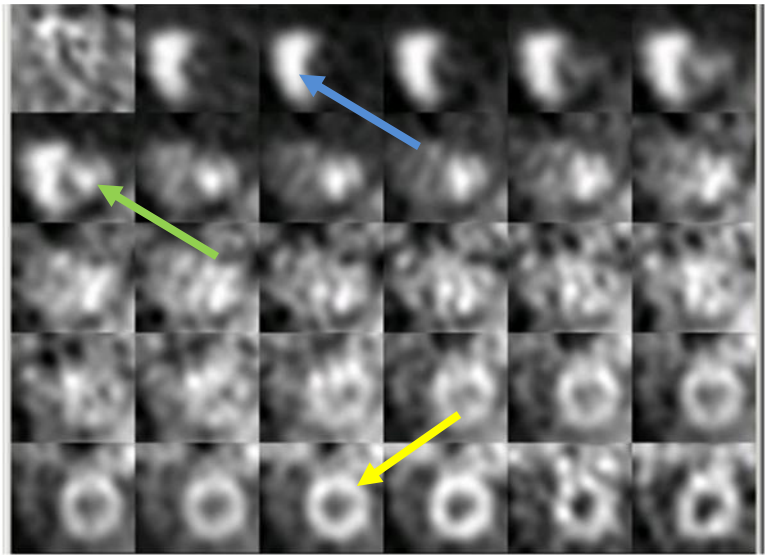

Figure 1. A mid-ventricular short-axis slice viewed over time following injection of N-13 ammonia. The upper left image is before activity reaches the heart. Proceeding left-to-right and down, the lower right image is the same mid-ventricular slice 5 minutes after injection. Note the activity first arrives into the right ventricle (blue arrow), then left ventricle (green arrow), then myocardial tissue (Yellow arrow).

32 regions of interest are automatically drawn to characterize the uptake (9 background, 4 concentric rings inside the left ventricle, 2 inside the right ventricle, and the standard 17 segment myocardial model). These regions are placed over each image volume in the time series to obtain the activity in each of the regions as a function of time. Examples graphs are shown in figure 2.

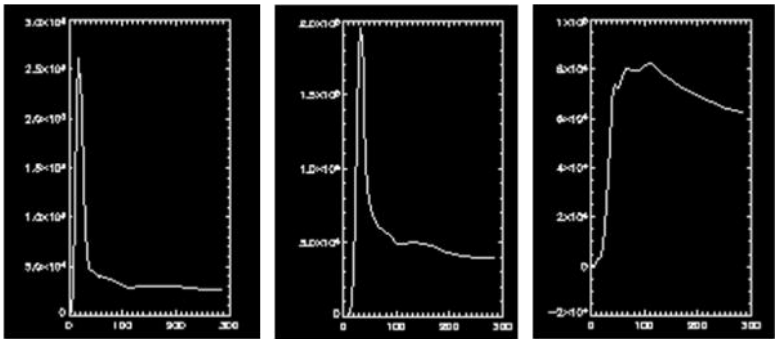

Figure 2. Time activity curves for the right and left ventricle, and myocardial tissue. Note the right ventricle (left curve) peaks first, followed by the left ventricle (middle curve), and then activity increases in the tissue (right curve).

Close inspection of the curves in figure 2 reveals that the measured activity in the left and right ventricles remains high (significantly above 0) for the duration of the study. However, direct blood sampling reveals that the amount of activity in the blood at the end of the study is minimal. Three phenomena cause this effect: 1) partial volume, 2) cardiac motion, and 3) tissue inhomogeneities. Collectively, these are termed spillover effects.

Before calculating myocardial blood flow, it is necessary to correct the measured data for spillover effects. To do this, it is assumed that the counts in each pixel arise from three "pure" and distinct curves (called factor curves) and that every measured curve can be reproduced as a weighted combination of the three pure curves. Factor analysis as presented by El Fakhri (El Fakhri 2005) is used to determine the three factor curves from the measured data. Figure 3 shows where the three factor curves are displayed in FlowTool. Knowing these factors, the spillover effects are removed from the measured curves leaving accurate estimates of the amount of activity in the blood and tissue within each pixel.

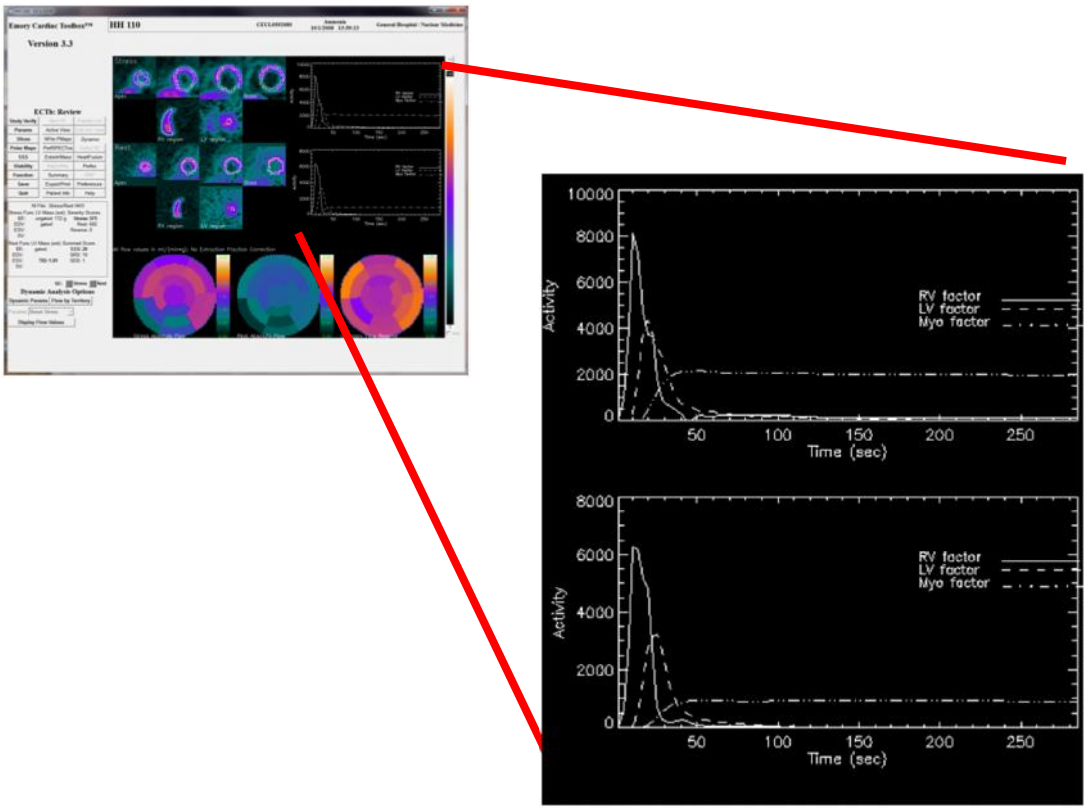

Figure 3. Presented are factor curves representing activity in the right and left ventricles, and the myocardial tissue following injection of Rb. Stress curves are on the top, rest on the bottom. Note activity enters the right ventricle first, then the left ventricle, and then the myocardial tissue. Once in the tissue activity remains for the duration of the study. Also note that the relative height of the tissue curve under stress is greater than during rest because of the greater blood flow.

Myocardial blood flow is calculated from the blood and tissue curves using the model described by Hutchins (Hutchins 1990) (figure 4). Activity starts in the blood. During a transit of the capillary bed, most of it crosses the capillary membrane and enters the tissue at a rate of FE (Flow times extraction). Most of this activity is irreversibly trapped, which forms the basis of the static and gated cardiac images of traditional PET cardiology. A small fraction of the activity returns to the blood and is transported away. Given the blood radioactivity (the left ventricle factor curve), the spillover corrected data for each region of interest, and the equations generated by the model depicted in figure 4, the value of FE can be calculated for each myocardial region. These are the values that are displayed by default on the displays in FlowTool.

Extraction fraction correction

The techniques referenced above are used to calculate FE. If E (the extraction) were equal to one for all flow values, then the myocardial blood flow, F, would be directly known. However, E is not unity for either ammonia or Rb. At rest, the extraction is approximately 0.84 for ammonia and 0.46 for Rb and

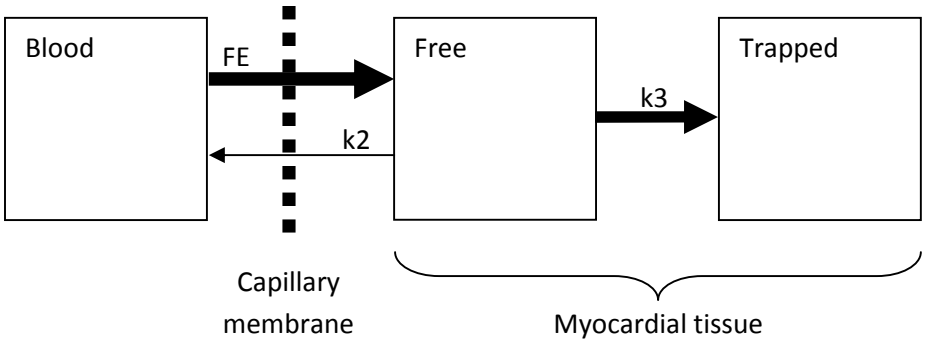

Figure 4. Compartment model used for calculating myocardial blood flow from spillover corrected measured PET data.

falls to 0.58 and 0.25 respectfully at maximal pharmacologic stress (Yoshida 1996). This explains why normal coronary flow reserve of approximately 4 (Holdright 1993) is measured as 2 with PET if the data is not corrected for the extraction fraction flow dependence.

Extraction fraction correction using the Yoshida equations can be included in the values presented in FlowTool by selecting this option on the preferences page. There may be good reasons for doing this such as comparison of CFR measurements from the PET and Cath labs. As a cautionary note, the correction is a multiplicative factor that increases both the flow value and its error. Hence, doing so has no benefit for distinguishing a significant difference between rest and stress measurements or for comparing a particular individual to population averages.

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