

Effect of filter cut-off frequency on the calculation of the left ventricular functional parameters derived from gated myocardial perfusion SPECT

^{1,2} Shereef Elmaghraby, MSc and ³ Magdy Khalil, PhD

¹ Nuclear Medicine Department, Kasr Al-Ainy University Hospital, Cairo, Egypt.

² Department of Physics, Faculty of Science, Al-Azhar University, Cairo, Egypt.

³ Medical Biophysics, Department of Physics, Faculty of Science, Helwan University, Cairo, Egypt

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Corresponding Author: Magdy Mohamed Khalil, PhD

Abstract

Aim: The purpose of the study was to investigate the influence of cut-off frequency by Butterworth and Hamming filters on the calculation of the left ventricular volumes (LVV) and ejection fraction (EF) estimated by Quantitative Gated SPECT (QGS) and Emory Cardiac Toolbox (ECTb).

Materials and Methods: Twenty patients were retrospectively collected for the study (14 males and 6 females). Mean age was 54 ± 11 y. Tc-99m tetrofosmin gated myocardial perfusion SPECT and equilibrium Gated Blood Pool (GBP) were performed for all patients within less than 2 weeks to each other. We utilized a geometric-count based (GCB) method for evaluating the LVV by GBP. Myocardial functional parameters from Gated SPECT imaging were calculated by QGS and ECTb software programs. A cut-off range of (0.25-0.50 cycle/cm) in Butterworth and (0.4-1.0 cycle/cm) in Hamming filters were used for prefiltering the gated SPECT images and the calculation of the myocardial functional parameters. The EDV, ESV, and EF from GBP and gated SPECT were tabulated and analyzed for comparison.

Results: ANOVA results revealed that there were no significant differences among volumes and EF calculated by ECTb across the cut-off values by Butterworth filter ($p=0.999$, $p=0.764$, and $p=0.299$ respectively) and also with QGS ($p=0.314$, 0.599 , and 0.874 respectively). Similar results were obtained by using Hamming filter. There was a trend to underestimate the volumes and overestimate the EF determined by QGS and ECTb at lower cut-off values by Butterworth and Hamming filters. Nevertheless, there were lower systematic differences between volumes and EF between GBP and gated SPECT as the cut-off increased. Both methods demonstrated good correlations with gated blood pool studies in the calculation of volumes and EF along the range of cut-off values provided by both filters. The EF determined by QGS and ECTb yielded a correlation range of (0.755-0.786) and (0.611-0.790) respectively with GBP. However, a correlation range of (0.734-0.797) and (0.728-0.914) respectively with Hamming filter.

Conclusion: The filter cut-off frequency has an impact on myocardial functional parameters estimated by QGS and ECTb algorithms. Both methods have a tendency to underestimate the ventricular volumes and overestimate the EF at lower cut-off frequencies. However, the estimation improves with an increase in the cut-off value with lower systematic differences. The filter cut-off has to be adjusted against a gold standard in an attempt to produce the most reliable measures of EDV, ESV, and EF.

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I. Introduction

Gated Single Photon Emission Computed Tomographic (gSPECT) imaging provides a simultaneous assessment of myocardial perfusion and function in one imaging setup. Left ventricular volumes and EF are important functional parameters for patients with coronary artery disease. Quantitative Gated SPECT (QGS) is one of algorithms that gained a wide spread among physicians for estimating the myocardial functional parameters (1,2). Emory Cardiac Toolbox (ECTb) is another validated software program that integrates myocardial perfusion and function in one application. (3). Both methods have achieved good correlations with each other (4) and with gold standard techniques (5,6); furthermore, they are reproducible and clinically acceptable for clinical routine use (7,8). Few studies were conducted to investigate the impact of filtering on gated data reconstruction and on the calculations of the myocardial functional parameters (9).

Butterworth is a common low pass filter that is used in many SPECT applications. Two parameters define the shape of the Butterworth filter, cut-off frequency and order. The filter cut-off suppresses high frequencies and maintains low values where important physiological information exists. In addition, the filter

has a resolution element provided by the slope of the cut-off frequency that is adjusted by the filter order. Hamming is also a low pass filter and is characterized by one parameter which is the cut-off frequency. By definition, the cut-off frequency is the value at which higher frequencies are suppressed and therefore denotes the bandwidth of the filter.

Recent guidelines by the joint group of the European Association of Nuclear Medicine and European Society of Cardiology have recommended that optimisation of filter parameters is best carried out empirically by each department based on their normal acquisition parameters. In addition, filter cut-offs should not be varied routinely (10). Since myocardial perfusion slices are more commonly interpreted by the visual sense, the observer comfort with the texture of the slices is therefore an important factor in determining the optimal cut-off value. However in gSPECT studies, it's more appropriate to select the filter and cut-off values on an objective basis. Determining the optimum cut-off value by using an ROC analysis is time consuming and requires extended efforts. In phantom studies, the cut-off value may be over- or underestimated as the simulation parameters may not appropriately represent the realistic conditions of data acquisition (11). The objective of the study was to investigate the influence of filter cut-off frequency provided by Butterworth and Hamming filters on left ventricular volumes and EF calculated by QGS and ECTb with respect to equilibrium gated blood pool.

II. Materials and Methods

Patients

Twenty patients were retrospectively collected for the study, 14 males and 6 females. A mean age of 54 ± 11 y. Patients' profile was (hypertensive, n=10), (Previous MI, n=4), (renal transplant, n=2), (Diabetes, n=6), (angina pectoris, n=4), (CABG, n=1). All patients underwent gated myocardial perfusion SPECT and equilibrium gated blood pool within less than 2 weeks to each other. Gated SPECT imaging was a two days protocol. Stress test was performed for 5 patients using treadmill exercise but 15 patients underwent pharmacological stress using dipyridamole (0.57mg/kg over 4 minutes infusion). Instructions were given to avoid coffee or caffeine containing products 24 hour before the test. A dose of 20-25 mCi Tc-99m tetrofosmin was injected at peak treadmill exercise or during peak pharmacologic vasodilation and the test continued for 60 sec after injection.

GE gamma camera in 101° geometry was used in data acquisition (Millennium MG, General Electric Medical systems, Milwaukee, WI). The acquisition arc extended from the right anterior oblique to the left posterior oblique. The acquisition time was 20sec/projection for a total of 36 projections using step-and-shoot mode.

The number of gates was 8-frames per cardiac cycle using R-wave trigger and acceptance window of 50%-150% of the mean pre-acquisition heart rate. The energy peak was 140 keV with 20% window. Low energy high resolution collimators were used. A matrix of 64×64 was used in data acquisition. Magnification was performed by a zoom factor of 1.33 which resulted in a pixel size of 6.78 mm. Patients with arrhythmia, atrial fibrillation, motion artifacts, high extra-cardiac activity were excluded from the study population.

Gated SPECT Processing

All data were transferred to the processing workstation Genie P&R (GE medical systems). The conventional filtered backprojection algorithm was used for image reconstruction. Projections were prefiltered using the Butterworth filter of cut-off 0.40 cycle/cm for the summed data. However, for the gated data we used a Hamming filter of cut-off frequencies 0.4-1.0 cycle/cm in a step of 0.10 cycle/cm and a Butterworth filter of cut-off frequencies 0.20-0.50 cycle/cm in a step of 0.05 cycle/cm. In all reconstructions, the Butterworth order was 7 (12). No attenuation or scatter correction was applied.

Gated Blood Pool (GBP)

Gated blood pool studies were performed for all patients who underwent myocardial perfusion imaging within less than two weeks to each other. Patient was initially injected by a pyrophosphate dissolved in 3 ml saline. Then a dose of 20-25 mCi Tc-99m was injected intravenously within 20-25 min post-pyrophosphate administration. Imaging started after 5 min post-Tc-99m injection using high resolution collimator adjusted in left anterior oblique position.

Images were taken with the best septal separation and time extended to 10 min. Matrix size was 64×64 with zoom factor of 1.6-2.0. The gating interval was 16 frames/cardiac cycle with rejection window of 30% of the mean pre-acquisition heart rate.

Geometric-Count based (GCB) Method

We used a geometric-count based (GCB) method for the evaluation of the left ventricular volumes. This method is recently reported and has some good features over the other methods in LV volume estimation. It

combines count based data with geometric based data assuming an ellipsoid left ventricular shape with identical short axes (13). The equation applied for EDV volume calculation is

$$EDV = 2cMC_{tot}/C_{max} \rightarrow 1$$

Where c (in cm) is a manually drawn short axis (one row pixel ROI) of the prolate ellipsoid in LAO 45° projection. M is the calibrated pixel size (cm²). C_{tot} and C_{max} are the total counts and the maximum pixel counts in the LV ROI respectively. Preliminary evaluation of GCB revealed better accuracy than a count based method, Massardo method (14), and achieved a good correlation with contrast ventriculography. Moreover; GCB method treated the background correction more efficiently by considering the geometric coordinates of the left ventricle (13). The method uses the formula:

$$C_{Bg} = [C_{mean} - (C_{max}F_{edge})]/(1-F_{edge})$$

to correct for the background. Where C_{mean} is the measured average number of counts in an average voxel along the LV edge, C_{max} is the maximal number of counts in the central voxel at the center of the LV taken proportional to the maximal depth of the ellipsoid, and F_{edge} is an averaged factor from four specific points, showing the ratio between the average depth of a prolate ellipsoid from its edge to the maximal depth of ellipsoid.

From a well drawn elliptical ROI around the LV; the edge, average, and maximum counts are calculated to give an appropriate measure of the background (13), and then formula 1 is applied to calculate the EDV. EF calculation is determined from the time-activity curve, and hence the ESV is easily calculated from the standard EF formula: $EF = 1 - (ESV/EDV)$.

We used imageJ (version 1.33p) software program which is a JAVA dependent image processing tool available at <http://rsb.info.nih.gov/ij> (developed by Wayne Rasband, National Institutes of Health, Bethesda, MD) for drawing the regions of interest and the calculation of the end-diastolic and end-systolic volumes. The EF was calculated using a standard application program available on the GE Xeleris workstation ('EF Analysis'). By using the GCB method, the mean EDV and ESV for the 20 patients was 109.0±38.0 ml and 56.45±29.9 ml respectively, but for EF, the mean value was 50.2±12.5%.

Quantitative Gated SPECT (QGS)

QGS is a 3-Dimensional algorithm for segmenting the left ventricle and extracting the functional information from the short axis data sets. It fits the myocardial mid-points with an ellipsoidal model using asymmetric Gaussian profiles (1,2). The endocardial and epicardial offsets are determined by given percentages of the sd calculated from the Gaussian fitting. In addition, the method utilizes the counts within and among frames in addition to the conservation of mass in outlining the myocardial borders (2).

Myocardial contouring is performed automatically without operator intervention. However, manual processing is optional when contouring process is not satisfactory. The endocardium, epicardium, and valve plane are calculated for each gating interval. Left ventricular cavity volumes are calculated by multiplying the individual pixel volume by the number of voxels contained in the three dimensional space bound by the endocardium and the valve plane. The largest and the smallest LV cavity volumes correspond to end-diastole and end-systole are calculated to calculate the left ventricular ejection fraction (1).

Emory Cardiac Toolbox (ECTb).

Emory Cardiac Toolbox is an integrated software application that provides functional and perfusion estimates in a single program. This method is based on the physics of partial volume and the systolic count change to estimate the myocardial boundaries utilizing the Fast Fourier Transform (15). It is clinically validated for functional parameters estimation (3,5-8). The software program works in 3D-space and is fully automated with the possibility to change the short axis radius and center.

Two coordinate systems are applied to sample the myocardium, cylindrical coordinate for the mid- and basal part of the myocardium and spherical coordinate for the apical portion. The program uses 8 frames per cardiac cycle (3,14). QGS and ECTb software packages obtained from system manufacturer (GE medical systems) were used in functional parameter estimation (EDV, ESV, and EF). All data were reconstructed and processed on Xeleris workstation (version 1.06, GE medical systems).

Statistical Analysis:

Data are represented as means and standard deviations. Student paired *t-test* was used for means comparison. The EFs were expressed in absolute values not as percentage of EF. Analysis of Variance (ANOVA) was used to search for significant differences among group means. Pearson correlation coefficient was applied to calculate the strength of association between two variables. A p value <0.05 was considered statistically significant. Data analysis was performed by a statistical software package for windows (SPSS Inc., Chicago, IL, USA, version 12.0)

III. Results

The effect of filter cut-off on the calculations of the left ventricular volumes and EF is graphically demonstrated in figures 1 and 2. ANOVA results revealed no significant differences among volumes (EDV, ESV) and EF calculated by ECTb across the cut-off values by Butterworth filter ($p=0.999$, $p=0.764$, and $p=0.299$ respectively). This was also true for QGS, no significant differences were found due to changing the filter cut-off. The p values were 0.314, 0.599, and 0.874 respectively. Furthermore, similar results were observed by using Hamming filter. No significant differences were observed for EDV, ESV, and EF calculated by QGS due to Hamming cut-off frequencies ($p=0.257$, 0.584, and 0.893 respectively) and for ECTb as well ($p=0.628$, 0.761, and 0.723 respectively). However, there was a trend to underestimate the volumes and overestimate the EF at lower cut-off values by both filters. As the cut-off increased there was a tendency to increase the volumes and to decrease the EF till the values reached a plateau. The effect of cut-off on the mean differences between gated blood pool and gSPECT for the calculation of the left ventricular volumes and EF is shown in figure 3.

Both methods demonstrated good correlations with gated blood pool studies in the calculation of volumes and EF along the range of cut-off values provided by both filters. Ranges of correlation coefficients are summarized in Table 1.

By Butterworth filter, the cut-off value at which the mean EDV by QGS was not significantly different from that by GBP was 0.30 cycle/cm (104.1±35.0 ml vs. 109.0±38.0 ml, $p=0.259$), but the EDV calculated by ECTb was not significantly different from that by GBP across all frequencies (Fig. 1A). The cut-off value at which the ESV by QGS was not significantly different from that by GBP was also 0.30 cycle/cm (52.2±28.8ml vs. 56.4±30.0ml, $p=0.136$). The ESV by ECTb was significantly lower than that by GBP across all cut-off values. In EF estimation, the cut-off value at which the EF by QGS was not significantly different from GBP was 0.25 cycle/cm (52.7±14.3% vs. 50.2±12.5%, $p=0.234$). However, the EF by ECTb overestimated significantly those values by GBP through all frequencies.

When Hamming filter was applied, the cut-off at which the mean EDV by QGS was marginally not significantly different from that by GBP was 0.6 cycle/cm (99.7±33.4 ml vs. 109.0±38.0 ml, $p=0.055$), but for ECTb, it was 0.5 cycle/cm (108.3±36.5 ml vs. 109.0±38.0 ml, $p=0.898$). In ESV estimation, the cut-off value at which QGS revealed a non-significant difference with GBP was 0.6 cycle/cm (51.1±29.1ml vs. 56.4±30.0 ml, $p=0.078$). ESV by ECTb was significantly lower than that by GBP throughout all cut-off frequencies. The cut-off value at which the EF by QGS was not significantly higher than that by GBP was 0.6 cycle/cm (53.8±13.7% vs. 50.2±12.5%, $p=0.100$). However, the EF by ECTb was significantly higher than that by GBP across all cut-off values.

Discussion

The introduction of fully automated gated SPECT software programs in nuclear medicine clinics has decreased inter-operator variations and improved patient diagnosis

Several factors are affecting the quality of myocardial tomographic images particularly when the study is ECG triggered. Some of these factors are reconstruction algorithm, injected dose, count density, imaging time, time after injection, energy corrections and the removal of scattered photons, zooming, matrix size, filter type, cut-off frequency. These factors, if not properly adjusted, may degrade the diagnostic accuracy of the quantitative algorithms

In the current study, we selected one of the factors, cut-off frequency, that is frequently employed in a very subjective way (16). In gated SPECT imaging, the data are noisier than the summed images due to temporal sampling and lower count statistics. One more source of noise is the use of ramp filter during backprojection. This filter magnifies high frequencies and increases the noise level in the reconstructed images. Low pass filters are commonly used to suppress this undesired amount of noise; however, this occurs on the expense of scarifying some image details.

Myocardial boundaries are classified as high frequency components and theoretically could be affected by low pass filtering. Low pass filters blur the edges by count smoothing and make the image details difficult to identify. QGS and ECTb are two commercially programs that depend on edge detection for volumes estimation and EF calculation. QGS method uses count profiles normally drawn from the cavity center on the myocardial walls. Asymmetrical Gaussian fit is used to determine the endocardial and epicardial offsets. ECTb utilizes the partial volume phenomenon and the intensity-size relationship (3,15).

ECTb assumes the ED at end-diastole as 10 mm, giving 5 mm inward and outward the mid-myocardial point. The EDV calculated by ECTb was not statistically affected by the Butterworth filter and most of cut-off values by Hamming filter. However, the EDV by QGS was significantly lower than that by GBP at lower frequencies. The heavy dependence of QGS on edge detection and normal count profiles might explain these findings.

Comparing the volumes estimated by gated SPECT to those calculated by GBP is not accurate enough in the clinical setting due to limitations of GBP for calculating left ventricular volumes. One of these is the 2D

nature of the acquisition and the geometric assumptions postulated to account for the depth. GBP scintigraphy assumes that the measured count rate is linearly related to the gamma-emitting blood volume and the cardiac cycle is strictly periodic. This assumption is almost holding true in stable conditions. Moreover, ROI demarcation, background subtraction, proper correction for attenuation and scattered photons may also reduce the accuracy of the measurements. However, the geometric-count based method applied in the current study has proved a better volume estimation than a count based method and achieved a good correlation with contrast left ventriculography in EDV and ESV measurements ($r=0.94$ and 0.90 respectively, both $p<0.01$) (13).

Despite the substantial limitations encountered by planar GBP for measuring the left ventricular volumes, a recent study revealed similar results when gated SPECT methods were compared to MRI (8). The EDV by ECTb was not significantly different from that by cardiac MRI, but the ESV was significantly lower than that by MRI. On the other hand, EDV by QGS was significantly lower and ESV was not significantly different from MRI. These findings agreed with our results using the two filters.

In a phantom study, the EDV and ESV by QGS showed an underestimation at lower cut-off values. The increase in cut-off values was associated with an increase in volumes to reach a plateau at the critical frequency 0.54 cycle/cm. The magnitude of underestimation was 17% and 8% for EDV and ESV respectively at the plateau level (17). This is also in agreement with our results; the mean differences by both methods using the two filters demonstrated a lower bias at higher cut-off values in comparison to the lower values (Fig. 3).

The EF by QGS and ECTb was higher than that by GBP at the lowest cut-off value, on average, by 6.9% and 19.3% respectively; however, these values were reduced to 0.9% and 9.0% respectively at the highest cut-off value using Butterworth filter. By Hamming filter, these values were 7.4% and 18.1% which then reduced to 1.6% and 11.3% respectively. Also, it was noted that both methods kept almost a constant difference between them along the range of cut-values studied.

The effect of filter cut-off on myocardial functional parameters calculated by Multidim program revealed similar findings to that found here. For EF, there was a higher mean difference ($-13.6\pm 13.1\%$) at lower cut-off values by Butterworth filter, which reduced to ($1.9\pm 7.9\%$) at higher frequencies when compared to GBP (9). Moreover, the authors reported correlations range of ($0.75-0.88$) between EF by gated SPECT and GBP similar to our results as illustrated in Table 1; however they have used Tl-201 as a radiotracer in patients with major myocardial infarction. Another study revealed correlation coefficients of ($0.81-0.86$) which is close to the results presented here; however six filters were investigated (18).

The updated guidelines by the American Society of Nuclear Cardiology have selected the value 0.55 Nyquist as a standard for processing gated SPECT images when 16 frames/cycle is used (12). This value is equivalent to 0.4 cycle/cm according to the pixel size used herein. As noted from the results and the demonstrating graphs, the cut-off 0.4 cycle/cm lies in the plateau region and yielded close results to gated blood pool. Wright et al also reported similar values using Butterworth filter at 0.4 Nyquist frequency (0.32 cycles/cm) which was in the plateau area of reproducibility (18). Similarly, in a dynamic cardiac phantom the standard deviations of functional parameters after repeated measurements were unaffected by different filters with critical frequencies of >0.39 cycles/cm. The precision of measurements improved with an increment in the cut-off value (17). By Nakajima et al, the underestimation of left ventricular volumes was 15% for 101 ml in a simulation study and the volume reached a plateau with cut-off >0.40 cycles/cm (19)

An ROC study revealed that a low cut-off value (0.14 pixel⁻¹ which was equivalent to 0.23 cycle/cm) outperformed the lower (0.12 pixel⁻¹) and higher frequencies (0.16 , 0.18 , and 0.22 pixel⁻¹) in detecting myocardial perfusion defects. This subjective evaluation of the optimal cut-off value might be underestimated due to the simulation nature of the study and the clinically irrelevant amount of noise generated (11). It's not necessarily to use the same cut-off value for both gated and un-gated data. Furthermore, the optimal value could differ according to the detection task.

It might be more convincing to perform a local-institutional study to search for differences in volume and EF calculations (in comparison to the available gold standard) due to different types of filters and cut-off frequencies. As the injected dose, imaging time, time after injection, collimation system, acquisition and processing parameters, patient populations, myocardial radiotracers, and imaging sequences (stress/rest) may vary substantially from center to another. An example of the patient population, we recently reported that Metz filter achieved better results than Butterworth in small left ventricles (20). Vera et al revealed significant differences among the filter frequencies applied on patients with major MI using Tl-201 as a radiotracer (9). Our results and others warrant the impact of filtering on the measurements of the end-diastolic, end-systolic and the derivation of the ejection fractions.

To our knowledge, this is the first study to investigate the influence of filter cut-off values on the estimation of functional parameters by ECTb. Although many articles were reported about QGS, no one included ECTb in the comparison. Also of interest, volume measurements were compared with planar GBP utilizing the newly reported GCB method.

IV. Conclusion

Our study showed that the two gated SPECT programs (QGS and ECTb) are consistent in the calculation of the left ventricular volumes and ejection fraction as a function of the cut-off frequency of the studied filters. Good correlations were found between volumes and ejection fraction estimated by the two methods and those obtained by the equilibrium gated blood pool studies (by applying the geometric count based method for volume estimation). Lower cut-off values underestimated the end-diastolic and end-systolic volumes but overestimated the EF. A mid-range cut off frequency that lies in the plateau region of measurements is thus recommended. The cut-off frequency has to be adjusted against a gold standard in an attempt to produce the most reliable estimates of EDV, ESV, and EF.

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Figure Legends

Figure 1. The effect of filter cut-off on the measurements of the EDV and ESV calculated by QGS and ECTb. (A) Butterworth filter. (B) Hamming filter. The mean EDV and ESV by GBP is 109 ± 38.0 ml. and 56.4 ± 29.9 ml. respectively.

Figure 2. The effect of filter cut-off on the measurements of the EF calculated by QGS and ECTb. (A) Butterworth filter. (B) Hamming filter. The mean EF by GBP is 50.2 ± 12.5 .

Figure 3. The mean differences between the EDV, ESV, and EF estimated by gated SPECT methods and those with GBP as a function of cut-off frequency. (A-B) Butterworth filter and (C-D) Hamming filter.

Table 1. Correlation results of EDV, ESV, and EF estimated by gated SPECT methods and GBP using the cut-off frequencies provided by Butterworth and Hamming filters.

	Functional parameters	QGS		ECTb	
		Corr. Coeff. range	Significance	Corr. Coeff. range	Significance
Butterworth filter	EDV	0.872-0.880	All p<0.0001	0.769-0.814	All p<0.0001
	ESV	0.912-0.921		0.873-0.910	
	EF	0.755-0.786		0.611-0.790	
Hamming filter	EDV	0.835-0.851	All p<0.0001	0.740-0.820	All p<0.0001
	ESV	0.904-0.915		0.847-0.895	
	EF	0.734-0.797		0.728-0.914	

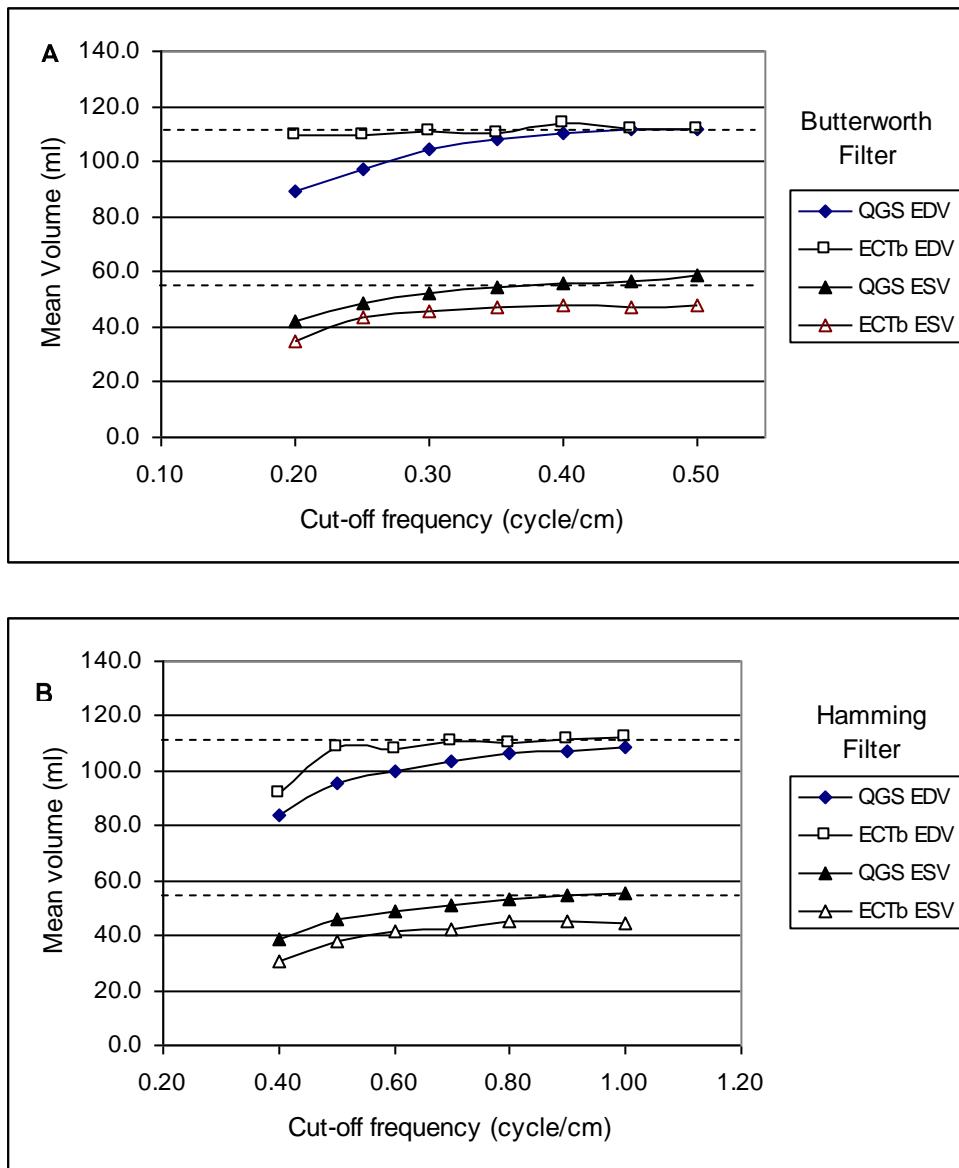


Figure 1

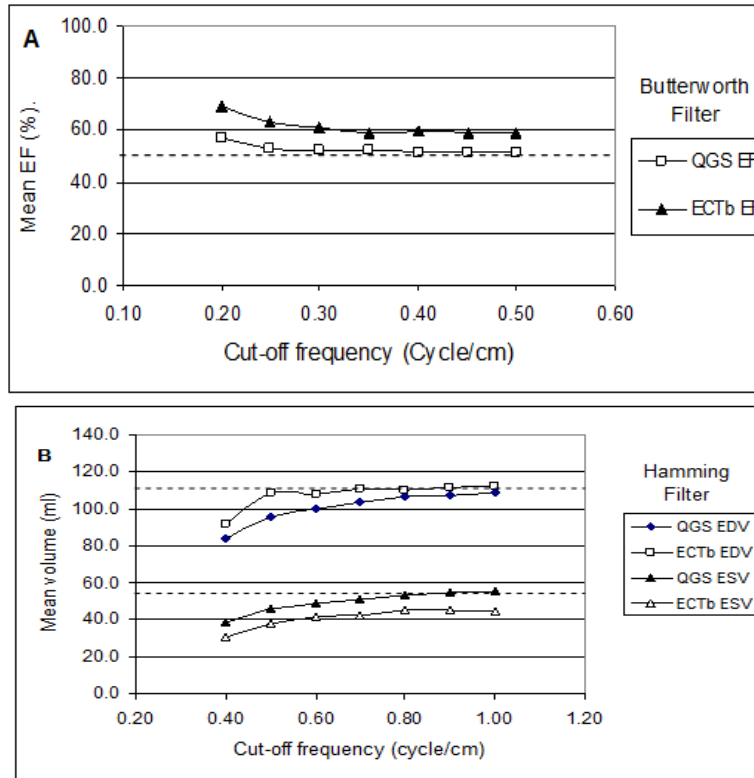


Figure 2

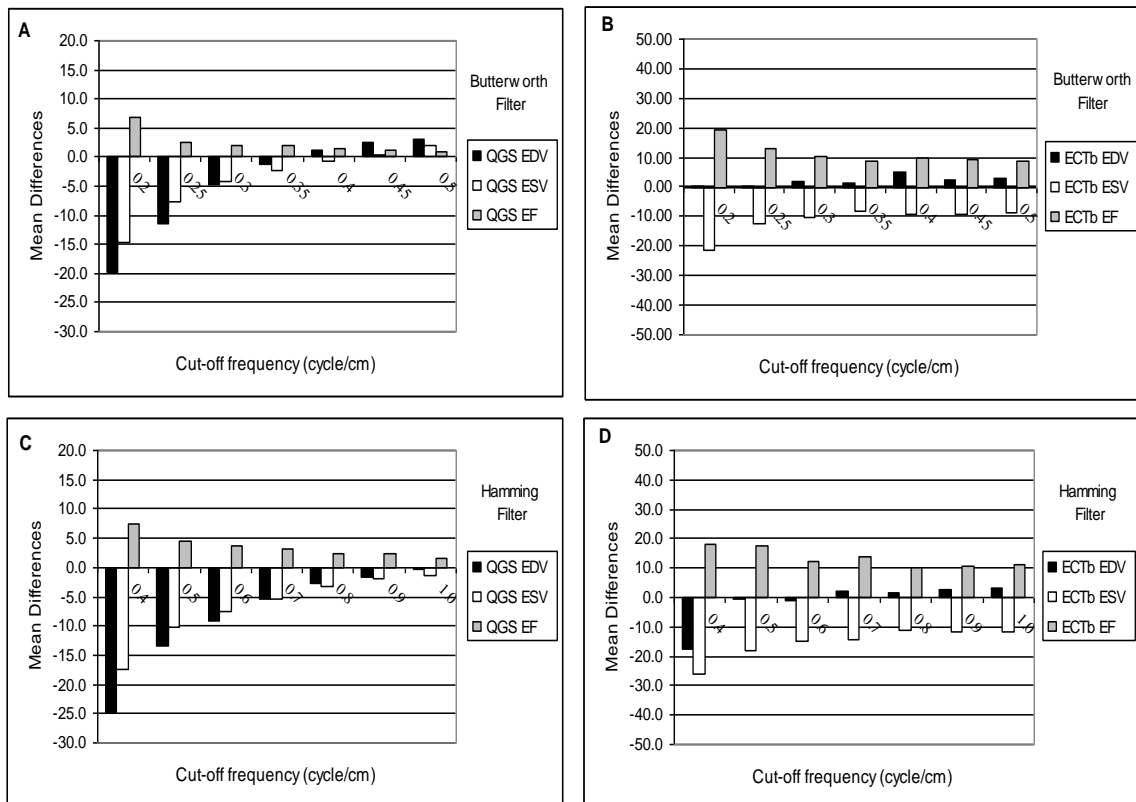


Figure 3

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