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Comparison study of temporal regularization methods for fully 5D reconstruction of cardiac gated dynamic SPECT †

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Abstract

Temporal regularization plays a critical role in cardiac gated dynamic SPECT reconstruction, of which the goal is to obtain an image sequence from a single acquisition which shows simultaneously both cardiac motion and tracer distribution change over the course of imaging (termed 5D). In our recent work, we explored two different approaches for temporal regularization of the dynamic activities in gated dynamic reconstruction without the use of fast camera rotation: one is the dynamic EM (dEM) approach which is imposed on the temporal trend of the time activity of each voxel, and the other is a B-spline modeling approach in which the time activity is regulated by a set of B-spline basis functions. In this work, we extend the B-spline approach to fully 5D reconstruction, and conduct a thorough quantitative comparison with the dEM approach. In evaluation of the reconstruction results, we apply a number of quantitative measures on two major aspects of the reconstructed dynamic images: 1) accuracy of the reconstructed activity distribution in the myocardium, and 2) ability of the reconstructed dynamic activities to differentiate perfusion defects from normal myocardial wall uptake. These measures include: mean square error (MSE), bias-variance analysis (BV), accuracy of time activity curves (TAC), contrast-to-noise ratio (CNR) of a defect, composite kinetic map of the LV wall, and perfusion defect detectability with channelized Hotelling observer (CHO). In the experiments, we simulated gated cardiac imaging with the NURBS-based cardiac-torso (NCAT) phantom and Tc99m-Teboroxime as the imaging agent, where acquisition with the equivalent of only three full camera rotations was used during the imaging period. The results show that both dEM and B-spline 5D could achieve similar overall accuracy in the myocardium in terms of MSE. However, compared to dEM 5D, the B-spline approach could achieve a more accurate reconstruction of the voxel time-activity curves; in particular, B-spline 5D could achieve a much smaller bias level in the early uptake stage of the imaging period. Furthermore, it could allow better separation of the perfusion defect from the normal at both the early and late stages of the imaging period.

Keywords

Gated SPECT; dynamic SPECT; 5D reconstruction; spatio-temporal

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1. Introduction

In nuclear cardiology, single photon emission computed tomography (SPECT) offers valuable information about both the radiotracer distribution in the myocardium and the ventricular function (Garcia 1996). In gated SPECT, the cardiac cycle is divided into a number of intervals according to the ECG signal in order to provide images portraying the contraction and relaxation of the myocardial wall during the cardiac cycle. Traditionally, the distribution of the tracer in a gated study is assumed constant over the course of imaging, and a single image is reconstructed for each gate period. However, for certain radiotracers with fast uptake and washout dynamics (e.g., Tc-99m labeled Teboroxime), it is more desirable to reconstruct the time-varying tracer distribution in the myocardium, because it could potentially provide valuable extra information for differentiation of myocardial flow abnormalities (Beanlands et al. 1992, Johnson 1994). In the literature there have been a number of techniques developed for dynamic SPECT reconstruction (e.g., (Farncombe 2000, Reutter et al. 2002)). However, most of these techniques, if not all, treat the organ of interest as motionless.

In recent years, 5D imaging has been investigated as a procedure that would allow reconstruction of dynamic images from a gated acquisition (Feng et al. 2006, Jin et al. 2006, Niu, Yang, Jin, Wernick & King 2010). The reconstruction problem in 5D can be particularly challenging in cardiac SPECT on several aspects. First, the projection data are available for only a few angular positions at a particular time instance, and thus, are far from being sufficient for reconstructing the dynamic images. Second, the data counts will now be divided among both the different gate intervals and the imaging time period, leading to even more imaging noise compared to the traditional gated SPECT.

Despite these challenges, we recently demonstrated in (Niu, Yang, Wernick & King 2010) that 5D reconstruction could lead to useful dynamic information for discriminating between normal wall and perfusion defects in terms of their timevarying activities. The study in (Niu, Yang, Wernick & King 2010) made use of a 5D reconstruction approach previously developed in (Jin et al. 2006, Niu, Yang, Jin, Wernick & King 2010), wherein the gated dynamic images were reconstructed jointly in order to exploit the correlation in the signal components among the different gate intervals. Furthermore, the dynamic EM (dEM) constraint first proposed in (Farncombe 2000), Feng et al. 2006) was used to regulate the time activities in the dynamic images.

Because of the importance of temporal regularization in 5D, we also explored in parallel an alternative approach in (Gravier et al. 2007) to regulate the time activity at a voxel location with a B-spline model. This approach was inspired by the work in (Nichols et al. 2002), in which B-spline basis functions were effectively used for dynamic image reconstruction in Positron emission tomography (PET). It was demonstrated in (Gravier et al. 2007) that the B-spline approach could greatly reduce the number of unknowns in modeling the dynamic images. For demonstration purposes the study in (Gravier et al. 2007) was with 2D image slices with a much simplified imaging model.

In this paper, our main purpose is to conduct a thorough comparison study of the B-spline approach and the dEM approach in order to determine the potential strength of each approach for 5D reconstruction. For this purpose we will also extend the B-spline approach in (Gravier et al. 2007) to fully 5D reconstruction wherein gated dynamic volumetric images are considered. In our evaluation study, we will use quantitative measures defined on two major aspects of the reconstruction results: 1) accuracy of the gated dynamic images in the myocardium, and 2) ability to separate between normal myocardium and perfusion defects according to their time-varying activities.

In our experiments, we conducted simulated gated cardiac imaging in which the ground truth is known for the purpose of quantitative evaluation. We used the NURBS-based cardiac-torso (NCAT) phantom (Segars 2001) and Tc99m-Teboroxime as the imaging agent, where acquisition with the equivalent of only three full camera rotations was used during the course of a 12 minute post-injection period.

The rest of the paper is organized as follows: the 5D imaging model for gated dynamic SPECT and the proposed B-spline approach are given in Section II. The evaluation criteria and methods are described in Section III. Experiment results are presented in Section IV, and conclusions are given in Section V.

2. Gated Dynamic SPECT Reconstruction

In this section, we first describe the general framework of 5D reconstruction, of which a key element is how to model the temporal dynamic image activities in order to combat the greatly under-determined nature of the reconstruction problem. We then present the two different temporal modeling approaches considered in this study: the B-spline modeling approach (Gravier et al. 2007) and the dEM approach (Niu, Yang, Jin, Wernick & King 2010, Jin et al. 2006). In the B-spline approach, the dynamic images are represented compactly by a small number of so-called control frames using a set of B-spline basis functions. In the dEM approach, the dynamic images are regulated by the temporal trend of the image activities at individual voxels.

2.1. 5D Reconstruction

As in traditional gated imaging, the acquired list-mode projection data are binned into K gate intervals by using the ECG signal. Following the notion in (Farncombe 2000), we use the angular incremental steps of the rotating SPECT camera to denote the progress of sample time t . The imaging data for a particular gate interval k , $k = 1, \dots, K$, are described by the following model

$$E[g_{t,k}] = H_t f_{t,k}, \quad t=1, \dots, T \quad (1)$$

where $g_{t,k}$, $f_{t,k}$ represent the projection data and the image, respectively, at time interval t , $E[\cdot]$ is the expectation operator, and H_t is the system matrix which is time-varying because of the rotation of the SPECT system. In this study the elements of the system matrix H_t are modeled as accounting for both the distance-dependent point spread function (PSF) and the attenuation effect of a SPECT system.

In the above model, for a given gate interval k , the entity $\{f_{t,k}, t = 1, \dots, T\}$ represents the dynamic tracer distribution over time t in the 3D volume when the cardiac phase is at interval k . Our goal is to reconstruct the dynamic images $\{f_{t,k}, t = 1, \dots, T\}$ for all gate intervals $k = 1, \dots, K$. Collectively, the set of unknowns $\{f_{t,k}, t = 1, \dots, T; k = 1, \dots, K\}$ represents a 5D quantity.

In the absence of fast camera rotation, the projection data $g_{t,k}$ in (1) are available for only a few projection angles (three in our experiments) during a particular time interval t . Thus, the reconstruction problem is greatly under-determined and, consequently, poses more challenges than in traditional gated SPECT where the tracer distribution is treated as constant during the course of imaging.

In 5D reconstruction, the collection of dynamic images $\{f_{t,k}, t = 1, \dots, T; k = 1, \dots, K\}$ is reconstructed jointly from the available projection data. Specifically, define

$\mathbf{f}_k = [f_{1,k}^T, \dots, f_{T,k}^T]^T$, i.e. a vector consisting of the dynamic images of gate k , $k = 1, \dots, K$;

similarly, define $\mathbf{g}_k = [g_{1,k}^T, \dots, g_{T,k}^T]^T$, which represents all the projection data for gate k . Moreover, define $\mathbf{H} = \text{diag} [H_1, H_2, \dots, H_T]$, i.e., a block diagonal matrix formed from the system matrix H_t collectively at $t = 1, \dots, T$. Then the dynamic imaging model in (1) can be rewritten as

$$E[\mathbf{g}_k] = \mathbf{H}\mathbf{f}_k, \quad k=1, \dots, K. \quad (2)$$

Moreover, let $\mathbf{F} = [\mathbf{f}_1^T, \dots, \mathbf{f}_K^T]^T$, a vector formed by the dynamic images of all gates; similarly, let $\mathbf{G} = [\mathbf{g}_1^T, \dots, \mathbf{g}_K^T]^T$. Then, the vector $\mathbf{F}$ is reconstructed using the following maximum *a posteriori* (MAP) estimation

$$\hat{\mathbf{F}} = \max_{\mathbf{F}} [\log p(\mathbf{G}|\mathbf{F}) + \log p(\mathbf{F})] \quad (3)$$

where $\log p(\mathbf{G}|\mathbf{F})$ is the likelihood function of the data $\mathbf{G}$ parameterized by $\mathbf{F}$, $p(\mathbf{F})$ is a prior distribution on $\mathbf{F}$. In this study, Poisson distribution is assumed for the likelihood function.

The prior term $p(\mathbf{F})$ in (3) is introduced to deal with the difficulty associated with insufficient projection data. It is defined in the form of both spatial and temporal regularization terms to exploit the similarity among the dynamic images. In this study we adopt a parametric modeling approach for $p(\mathbf{F})$, in which the time activities at individual voxels are regularized by a set of B-spline basis functions. For comparison, we will also consider a non-parametric approach, the dEM approach previously developed in (Niu, Yang, Jin, Wernick & King 2010).

2.2. 5D B-spline Reconstruction

Following our previous development in (Gravier et al. 2007), we model the time activity at each individual voxel of the dynamic images by a set of cubic B-splines (Boor 1978) as in (Nichols et al. 2002). Mathematically, for voxel j , the dynamic image $f_{t,k}$ of gate k and time t is written as:

$$f_{t,k}(j) = \sum_{m=1}^M b_{t,m} w_{m,k}(j), \quad k=1, \dots, K, j=1, \dots, N \quad (4)$$

where $b_{t,m}$ is the scalar value of the m^{th} spline basis function at time t , $w_{m,k}$ is a vector formed by the weights (called *control points*) of all voxels associated with basis function $b_{t,m}$, M is the total number of basis functions used, and N is the total number of voxels. It is noted that in the above a common set of basis functions is used for all the different voxels and gates.

With the model in (4), the set of dynamic images $\{f_{t,k}, t=1, \dots, T\}$ of gate k is now represented by a set of control points $\{w_{m,k}, m=1, \dots, M\}$. The problem then becomes how to determine the control points $w_{m,k}$ from the projection data. Once the control points are determined, the dynamic images are subsequently obtained through interpolation using (4). Typically we have $M \ll T$; thus, the number of unknowns in the B-spline model is much smaller than that in original dynamic images in (1). In our experiments, we used $M=6$ control points compared to $T=64$ time points. This can greatly reduce the memory requirement, making the B-spline approach more attractive in practical implementation.

For convenience, let $\mathbf{W} \equiv \{w_{m,k}, m = 1, \dots, M, k = 1, \dots, K\}$, i.e., a vector consisting of the control points of all gates. The MAP estimate for $\mathbf{F}$ in (3) can be rewritten in terms of the control points $\mathbf{W}$ as

$$\hat{\mathbf{W}} = \arg \max_{\mathbf{W}} [\log p(\mathbf{G}|\mathbf{W}) + \log p(\mathbf{W})] \quad (5)$$

where $p(\mathbf{G}|\mathbf{W})$ is the likelihood function of $\mathbf{G}$ parameterized by $\mathbf{W}$, $p(\mathbf{W})$ is a prior distribution on $\mathbf{W}$.

We use a separable Gibbs prior for $p(\mathbf{W})$ as following

$$p(W) \propto \exp[-\beta_s U_s(W) - \beta_\tau U_\tau(W)] \quad (6)$$

where $U_s(\mathbf{W})$ and $U_\tau(\mathbf{W})$ are two energy functions defined over space and gate intervals, respectively, β_s and β_τ are their corresponding weighting factors.

The term $U_s(\mathbf{W})$ in (6) is used to enforce local spatial smoothness within each image frame. It is defined as

$$U_s(W) = \sum_{k=1}^K \sum_{m=1}^M \sum_{j=1}^N \sum_{i \in \eta_j} [w_{m,k}(j) - w_{m,k}(i)]^2 \quad (7)$$

where η_j is the unit-distance neighborhood around voxel j , and N is the number of voxels in $w_{m,k}$.

The term $U_\tau(\mathbf{W})$ in (6) is used to enforce temporal smoothness along the motion trajectories across the different gates. It is defined as

$$U_\tau(W) = \sum_{k=1}^K \sum_{m=1}^M \|w_{m,k} - \sum_{l=1, l \neq k}^K q_{l \rightarrow k} \hat{w}_{m,l \rightarrow k}\|^2 \quad (8)$$

where $\hat{w}_{m,l \rightarrow k}$ denotes the motion-compensated prediction of control points $w_{m,k}$ in gate k from its neighboring gate l , and $q_{l \rightarrow k}$ is a weighting parameter so defined that temporally neighboring gates contribute more to the prediction of the current frame than those gates further apart. In our experiments, the following was used for $q_{l \rightarrow k}$:

$$q_{l \rightarrow k} = C \left(1 - \left|\frac{l-k}{K}\right|\right)^3, \quad (9)$$

where C is a normalizing constant so that the sum of $q_{l \rightarrow k}$ over all neighboring frames l is unity. The temporal term in (8) is modified from what was previously used in (Gravier et al. 2007), where the prediction of the current frame was predominantly from its two neighboring frames; in comparison, the weighting coefficients in (9) allow for more contributions from other temporal frames in the prediction.

In this study we used the iterative BSREM-II algorithm as in (Ahn & Fessler 2003, Gravier et al. 2007) to solve the optimization problem in (5). The BSREM-II algorithm is known to be globally-convergent and typically faster than non-ordered-subset algorithms. Without interrupting the flow of the presentation, we provide the details of the reconstruction algorithm in Appendix A.

2.3. 5D dEM Reconstruction

For comparison, here we briefly describe the dEM constraint approach previously developed in (Niu, Yang, Jin, Wernick & King 2010). In this approach, the time activities at individual voxels were regulated by Farncombe's dEM constraint (Farncombe 2000). That is, at each voxel the trend of the dynamic activity can only be either constant, increasing only, decreasing only, or first increasing and then decreasing. Unlike the B-spline approach above, the dEM constraint does not assume a specific parametric form on the time activities. With dEM constraint, the dynamic activity at a voxel is expressed in the form of its temporal increments (for increasing trend) or decrements (for decreasing trend). The image reconstruction is through estimating these temporal increments or decrements.

Let A denote the differential operator for computing the temporal increment (or decrement) in $\mathbf{F} = [\mathbf{f}_1^T, \dots, \mathbf{f}_K^T]^T$, and let $\tilde{\mathbf{F}}$ denote the transformed incremental (or decremental) form of $\mathbf{F}$, i.e.,

$$\tilde{\mathbf{F}} = A\mathbf{F}. \quad (10)$$

Then the dEM constraint is simply written as $\tilde{\mathbf{F}} \geq \mathbf{0}$.

The incremental vector $\tilde{\mathbf{F}}$ is reconstructed using the following MAP estimation

$$\hat{\tilde{\mathbf{F}}} = \max_{\tilde{\mathbf{F}} \geq \mathbf{0}} [\log p(\mathbf{G}|\tilde{\mathbf{F}}) + \log p(\mathbf{F})] \quad (11)$$

where $\log p(\mathbf{G}|\tilde{\mathbf{F}})$ is the likelihood function of the data $\mathbf{G}$ parameterized by $\tilde{\mathbf{F}}$, $p(\mathbf{F})$ is a prior distribution on $\mathbf{F}$.

As in the case of B-spline 5D above, we use a separable Gibbs prior for $p(\mathbf{F})$:

$$p(\mathbf{F}) \propto \exp[-\beta_s U_s(\mathbf{F}) - \beta_\tau U_\tau(\mathbf{F})] \quad (12)$$

where $U_s(\mathbf{F})$ and $U_\tau(\mathbf{F})$ are two energy functions defined over space and gate intervals, respectively, β_s and β_τ are their corresponding weighting factors. Once $\tilde{\mathbf{F}}$ is obtained, the image frames are determined as $\mathbf{F} = A^{-1}\tilde{\mathbf{F}}$. More details of this algorithm can be found in (Niu, Yang, Jin, Wernick & King 2010).

3. Evaluation Methods

3.1. Data sets

In this study, we use simulated cardiac gated dynamic imaging in which the ground truth is known for quantitative evaluation. In our experiments, we used the NURBSbased cardiac-torso (NCAT) v2.0 phantom (Segars 2001) with a tracer-kinetic model simulating imaging with Tc99m labeled Teboroxime, as shown in Fig. 1, where different time activities were introduced among the different organs as in (Feng et al. 2006). Note that the LV blood pool is shown separately from the rest of the myocardium. The right ventricle (RV) blood pool was set to have the same time activities as LV in the experiment. A perfusion defect was introduced in the anterior wall of the left ventricle (LV), as illustrated in Fig. 2 in a short-axis slice of the LV for gate #1. The dynamic activity of the defect is shown in Fig. 1, which is noted to have slower uptake and washout rates than the normal myocardium. It is also noted that there is a high concentration in the liver.

In our simulation, a triple-head camera system with the heads at 120° apart from each other was used, and 64 rotation stops covering a total of 360° by each head with 64 × 64

projection bins at each stop were used during 12 minute data acquisition as in a clinical study. A total of eight gates were used. The field of view was 40.5 cm. The system had a distance dependent blur of approximately 13 mm full width at half-maximum (FWHM) at the center of rotation. The attenuation map from NCAT phantom was used for the simulation data. An analytical projector model was used to generate the projection data, for which both depth-dependent blur and attenuation were included. Poisson noise was introduced corresponding to a count level of 8 million total counts (for all projections and over all time). The same analytic projector was used for the image reconstruction. We assumed perfect scatter correction in this study, as our primary focus is on comparing the relative performance of the reconstruction algorithms at this early stage of development. While inclusion of degrading factors such as scatter and projector modeling error will degrade the reconstruction performance, they tend to impact the different methods in the same way and their relative ordering in performance is expected to remain the same.

In our experiments, the reconstruction algorithms were tested using 30 different noise realizations. For each noise run, a sequence of dynamic volumetric images was obtained over 64 time points during the 12 minute period for all the eight gates.

3.2. Reconstruction Methods

To compare the effects of temporal regularization methods, the following different methods were used to reconstruct the gated dynamic images: 1) fully 5D B-spline reconstruction, and 2) fully 5D dEM reconstruction. As reference for comparison, the noiseless images (reconstructed with EM from complete, noiseless projection data) were used (denoted as “Ideal”). As noted above, both depth-dependent blur and attenuation were directly modeled in the reconstruction.

In both 5D methods, the image motion in the motion-compensated gate smoothing prior in (6) and (12) was determined from the noisy projection data. In each method, the dynamic sequence was first reconstructed separately for each gate interval, i.e., $\beta_t = 0$ in (6) or (12), which corresponds to reconstruction of individual gates using spatial smoothing alone. The resulting images were then summed along the dynamic time axis to get a static image for each gate frame, which were subsequently processed by a lowpass filter (order-3 Butterworth filter with 0.2 cycles/voxel cutoff frequency). Afterward, the 3D optical flow method was applied to these summed images to estimate the motion between the different gate frames (Gravier et al. 2006).

For the cubic B-spline model in (4), we selected the number of knots and their temporal position as in (Gravier et al. 2007), in which two internal knots were used to represent the dynamic time activity of the tracer, one was placed during the initial uptake period of the heart, the other was placed near the start of the washout period. The six basis functions were then generated with the knot placement at [0, 0, 0, 0, 0.5, 1.5, 12, 12, 12, 12] min. Note that clamped knots were used at both ends of the imaging period, i.e., at 0 and 12, each having a multiplicity of 4. The two internal knots at 0.5 and 1.5 were placed nonuniformly toward the early stage of the imaging period in consideration of the fast changes in image activities therein.

3.3. Reconstruction Accuracy Evaluation

We first evaluated the reconstruction accuracy of the gated dynamic images using several quantitative measures as described below.

3.3.1. Mean square error (MSE)—To quantify the overall reconstruction accuracy of the myocardium, we computed the MSE of the reconstructed dynamic images of the

myocardium over the entire imaging period. The MSE is a direct measure of the accuracy of the reconstructed image values in the presence of imaging noise. In our experiment, we used a volume of $20 \times 19 \times 17$ voxels which contains the entire myocardium for MSE evaluation (of which three slices are shown in Fig. 3). A detailed definition of MSE is given in Appendix B.

3.3.2. Bias-variance analysis—We also quantified the regional accuracy of the heart wall in the reconstructed images using bias-variance analysis. Two ROIs selected on the LV were used (one normal, one defect; each of size $2 \times 2 \times 2$), as shown in Fig. 3. The accuracy of these ROIs was quantified for different stages of the dynamic images (early, middle, and late). The results were summarized by using bias-standard deviation plots. A detailed description of the bias-variance procedure used is given in Appendix B.

3.3.3. Time activity curve (TAC)—We also computed the regional TACs of the LV in the reconstructed gated dynamic images. The TACs were computed for the same two ROIs (normal and defect) as used in the bias-variance analysis above (Fig. 3) over 30 noise realizations. The TACs are used to demonstrate whether the reconstructed dynamic images can discriminate the regional time-varying tracer distribution of the LV over time.

3.3.4. LV ejection fraction (LVEF)—We also quantified the reconstruction using ejection fraction (EF), a measure pertinent to clinical assessment of LV functions. To obtain LVEF, a reconstructed 5D image sequence was first collapsed into a gated sequence by summing along the dynamic time axis; the clinical software package 4DMSPECT was then used to compute the EF from this collapsed sequence (Niu, Yang, Wernick & King 2010).

3.4. Defect Detectability from Dynamic Activities

We also quantified the detectability of perfusion defects in the gated dynamic images using several quantitative measures. These measures were used to quantify the defect both at a particular time point and over the imaging period as a whole.

3.4.1. Contrast-to-noise ratio (CNR)—To quantify the visibility of a perfusion defect in the presence of noise, we computed the CNR for the defect relative to the LV over the course of imaging period. In our experiments the dynamic images of the first gate interval (near end diastole) was used; the defect ROI is shown in Fig. 3. Both the maximum and average CNR values over the dynamic time were computed for this defect. A detailed definition of these quantities is given in Appendix B.

3.4.2. Channelized Hotelling observer (CHO)—To quantify lesion detectability in the reconstructed images, a channelized Hotelling observer (CHO) was used to detect the defect at each different time point in the first gate. In the CHO, four rotationally symmetric, non-overlapping input channels were used and internal noise was included as in (Narayanan et al. 2002). A total of 60 noise realizations (30 lesion-present and 30 lesion-absent) were used. The detection performance was summarized using the area under the receiver operating characteristic (ROC) curve. These ROC studies represented a “signal-known exactly” and “background-known exactly” observer study. The noise parameter in the CHO was set from our previous study of gated SPECT images (Jin et al. 2009).

3.4.3. Composite kinetic map—To characterize the dynamic information that is salient for detection of perfusion defects, we also computed a composite kinetic map from the gated dynamic images. The composite map is formed from the uptake and washout rate constants extracted from the reconstructed TACs (Niu, Yang, Wernick & King 2010). Specifically, at a voxel j the kinetic composite map is defined as:

$$C(j) \triangleq \alpha' \mathbf{k}(j) = \alpha_1 k_{12}(j) + \alpha_2 k_{21}(j), \quad (13)$$

where k_{21} and k_{12} denote, respectively, the uptake and washout rate constants from a two-compartmental model (Smith et al. 1996, Chiao et al. 1994), and α is the Fisher discriminant vector between the normal and defect classes (Niu, Yang, Wernick & King 2010).

4. Results and Discussions

4.1. Reconstruction Accuracy

4.1.1. MSE—In Fig. 4(a) we show the MSE results of the reconstructed myocardium by B-spline 5D reconstruction; in this plot, each curve was obtained by varying the spatial parameter $\beta_s = [0, 0.5, 1, 2] \times 10^{-4}$ while the gate parameter β_τ was held at a constant value. These results were obtained from an average of 30 different noise realizations. The results in Fig. 4(a) show that use of gate smoothing prior (i.e., $\beta_\tau = 0$) resulted in more accurate reconstruction of the myocardium than spatial-only smoothing (i.e., $\beta_\tau = 0$). The largest error was obtained when neither spatial nor gate smoothing was used (i.e., $\beta_s = 0$ and $\beta_\tau = 0$); on the contrary, the best MSE=0.0403 was achieved with $\beta_\tau = 1 \times 10^{-3}$, $\beta_s = 5 \times 10^{-5}$. Moreover, it is noted that with gate smoothing the benefit of spatial smoothing becomes diminished due to its blurring effect. That is, while spatial smoothing can be effective for noise reduction, it also results in resolution loss. With the limited thickness of the LV wall, the effect on noise reduction is outweighed by that of spatial blurring.

For comparison, we show in Fig. 4(b) the MSE results obtained by dEM 5D reconstruction. For each curve the spatial parameter was varied as $\beta_s = [0, 0.2, 0.4, 1] \times 10^{-6}$. The best MSE=0.0433 was obtained with $\beta_\tau = 3 \times 10^{-5}$, $\beta_s = 2 \times 10^{-7}$. Interestingly, this MSE level is similar to that of B-spline 5D above.

4.1.2. Bias-variance—In Fig. 5 we show the bias and standard-deviation plots for the normal ROI on the LV wall (Fig. 3) obtained by B-spline 5D. These plots were given for the dynamic images at $t = 1.78$ min, 4.78 min, and 10.03 min (which represent the early, middle and late stages of the imaging period). These results were obtained from 30 noise realizations. As in Fig. 4, each curve in Fig. 5 was obtained by varying $\beta_s = [0, 0.5, 1, 2] \times 10^{-4}$. For comparison, we also show in Fig. 5 the corresponding bias and standard-deviation plots obtained with dEM 5D. The spatial parameter was varied as $\beta_s = [0, 0.2, 0.4, 1] \times 10^{-6}$. It is noted that the spatial parameter β_s was much larger in B-spline than in dEM. This is because the spatial term in (7) is defined over the number of knots M which is far smaller than the number of time points T .

From these results it can be seen that use of spatial smoothing reduces the variance at the expense of increased bias; at a given bias level, use of gate prior can significantly reduce the variance. Moreover, the reconstructed images exhibit a larger bias at the early stage of the imaging period than in later stages. We believe that this is mainly attributed to the slow camera rotation compared to the fast activity change during the early stage.

It is also noted that at the early stage, the bias level with B-spline 5D is much lower than that of dEM 5D. In the late stage, B-spline 5D shows an increase in the variance level compared to dEM 5D. This could be due to the fact that the B-spline basis functions have compact support, which would allow for better adaption to the signal change (hence reduced bias, but also potentially more sensitive to noise.)

4.1.3. TACs—In Fig. 6(a) we show the TACs obtained by B-spline 5D for the defect and normal ROIs in the myocardium (shown in Fig. 3). These results were obtained from 30

noise realizations, and the parameters from the optimal MSE were used (i.e., $\beta_s = 5 \times 10^{-5}$, $\beta_\tau = 1 \times 10^{-3}$). For comparison, the TACs of the ideal reference are also shown. In addition, the corresponding TACs obtained by dEM 5D ($\beta_s = 2 \times 10^{-7}$, $\beta_\tau = 3 \times 10^{-5}$) are given in Fig. 6(b).

As can be seen, the reconstructed dynamic images by both B-spline 5D and dEM 5D could yield a good separation between the normal and perfusion defect TACs. However, B-spline 5D could achieve a smaller bias than dEM 5D at the early stage of the imaging period. Interestingly, this is consistent with the bias-variance results in Fig. 5 above. Furthermore, B-spline 5D could also achieve a larger separation between the normal and defect at the late stage (for t after 8 min) than dEM 5D due to the reduced bias in the reconstructed defect TACs. Note that such a larger separation also corresponds to a higher contrast of the defect from the normal in the reconstruction. As will be seen in the CHO results below, this improved contrast also leads to better lesion detectability.

It is also noted that in Fig. 6 for both methods the crossing time at which normal and defect myocardium have equal activity concentrations is different from that of the ideal case. However, in the work of (Feng et al. 2006), a good agreement was demonstrated in the reconstructed images. We believe that this difference is likely due to the particular choice of the spatial smoothing parameter. As shown in the bias-variance results in Fig. 5 above, the bias levels vary both at different stages of the imaging period and with the choice of the spatial parameter. The TAC results shown in Fig. 6 were based on the optimal MSE setting, which may not be optimal for the bias level around the crossing time point.

4.1.4. LVEF—With 30 noise realizations, the obtained average EF is 59.5 (6.19) for B-spline 5D and 57.25 (5.12) for dEM 5D, where the standard deviation values are given in parentheses. As reference, the ground truth of EF from the NCAT phantom is 59.71. It is observed that both B-spline 5D and dEM 5D could lead to fairly accurate estimates of the EF. These results demonstrate that the gated dynamic images could also yield valid information for LV function assessment.

4.2. Defect Detectability

4.2.1. CNR—To quantify the visibility of the perfusion defect in the dynamic images, we computed the CNR of the defect region relative to its surrounding normal myocardium. The results are summarized in Table 1. These results were obtained from 30 noise realizations when the defect was present. Both the maximum and average CNR values over the imaging period are given in Table 1; their standard deviation values are included in parentheses. It is noted that B-spline 5D yields much higher CNR values for the defect than dEM 5D. These results indicate that B-spline 5D could allow for better defect detection than dEM 5D, as confirmed by the CHO results below.

4.2.2. CHO detectability—The CHO was applied to a slice of dynamic images of the myocardium (slice #21) in the first gate. As an illustration, Fig. 7 shows the tracer distribution of this slice at three different time points. The CHO was applied to detect the defect in the dynamic images at different time points. We summarize in Fig. 8 the lesion detectability results from the reconstructed dynamic images by B-spline 5D, where the area under the ROC curve (A_z) is plotted for the entire imaging period. For comparison, results are also shown similarly for dEM 5D. The error bars indicate the standard deviations.

As can be seen, with B-spline 5D the best detection results occur at both the early and late stages of the imaging period. This is consistent with the TAC results observed earlier in Fig. 6, where the difference in image activity is more evident between normal and defect regions in early and late stages.

Furthermore, the results in Fig. 8 also show that B-spline 5D can yield consistently higher Az values than dEM 5D during both the early and late stages. Interestingly, this is also in agreement with the both the TAC results in Fig. 6 and the CNR results in Table 1.

4.3. Reconstructed Images

4.3.1. Gated dynamic images—We show in Fig. 9 a set of dynamic images of the LV volume in short-axis view for a number of selected gates and time points reconstructed from a typical noise realization by B-spline 5D ($\beta_s = 5 \times 10^{-5}$, $\beta_t = 1 \times 10^{-3}$) and dEM 5D ($\beta_s = 2 \times 10^{-7}$, $\beta_t = 3 \times 10^{-5}$). For comparison, the ideal reference images are also shown. For clarity, only the heart region is shown for four different gates (#1, #3, #5, #7) and nine time points of the imaging period. The images along the horizontal direction show the effect of cardiac motion, while along the vertical direction they show the effect of tracer dynamics over time. The dynamic images in a volume were normalized to have the maximum intensity in each method.

From Fig. 9 it is noted that the perfusion defect region (Fig. 2) was initially dimmer than the rest of the LV wall in the early stage, reflecting slower uptake; it then reversed to become brighter in the late stage, reflecting slower washout. This is particularly more evident in the B-spline 5D images than in the dEM 5D images. The B-spline 5D images are also notably closer to the ideal reference during both the early and late stages. These results were consistent with both the dynamic TACs in Fig. 1 and the CHO in Fig. 8.

4.3.2. Composite kinetic parametric map—In Fig. 10(a) we show the composite kinetic map obtained from a typical noise realization for the same slice in Fig. 2 by B-spline 5D. For comparison, the results are shown for both when the defect was present and when it was absent. In this map the image intensity is notably lower in the defect region than in the normal myocardium, reflecting the difference in tracer uptake and washout parameters. The extent of the defect is noted to be in good agreement with the dynamic images in Fig. 9. For comparison, in Fig. 10(b) we also show the composite kinetic map obtained by dEM 5D. Note that these parametric maps were shown using the same colormap as for conventional SPECT images.

5. Conclusions

In this study we further developed a B-spline regularization approach for fully 5D reconstruction in gated dynamic cardiac SPECT imaging without fast camera rotation. We conducted a thorough quantitative evaluation study of the B-spline approach, and compared it with a recently developed fully 5D approach based on dynamic EM (dEM) regularization. Our results demonstrate that both B-spline and dEM 5D could obtain a sequence of gated dynamic images from a single acquisition which can provide information simultaneously for both time-varying tracer distribution and ejection fraction. While both B-spline and dEM could achieve similar overall error level in reconstruction, B-spline 5D could achieve more accurate reconstruction of the dynamic activities in the myocardium than dEM 5D. In particular, it could yield a much lower bias level in the reconstructed myocardium at the early uptake stage of the imaging period. Measured by a channelized Hotelling observer (CHO), B-spline 5D could consistently lead to better lesion detectability than dEM 5D, with the most improvement occurring at both the early and late stages of the imaging period. Encouraged by these results, in future studies we plan to further develop and evaluate these reconstruction approaches by inclusion of other degrading factors in SPECT toward the ultimate goal of making 5D imaging a useful clinical tool.

Appendix A: B-spline 5D Reconstruction Algorithm

In the BSREM-II algorithm (Ahn & Fessler 2003, Gravier et al. 2007), we first divide the entire set of projection data $\mathbf{G}$ into a number of subsets. With t denoting the angular rotating steps of the SPECT camera, it is convenient to divide the projection data according to t . Assuming a total of L subsets used, the objective function in (5) is accordingly decomposed

into $J(\mathbf{W}) = \sum_{l=1}^L J_l(\mathbf{W})$, in which the sub-objective function $J_l(\mathbf{W})$ of subset l is defined as

$$J_l(\mathbf{W}) = \sum_{i \in S_l} \sum_{k=1}^K \sum_{j=1}^B \left\{ -b_{t,m} \sum_{j=1}^N H_t(i, j) w_{m,k}(j) + g_{t,k}(i) \log \left[b_{t,m} \sum_{j=1}^N H_t(i, j) w_{m,k}(j) \right] \right\} - \frac{1}{L} \beta_s U_s(\mathbf{W}) - \frac{1}{L} \beta_\tau U_\tau(\mathbf{W}) \quad (14)$$

where S_l denotes the collection of angular positions in subset l , and B is the number of projection bins.

During each iteration, the elements of $\mathbf{W}$ are updated as follows

$$w_{m,k}^{n,l} = P \left[w_{m,k}^{n,l-1} + \alpha_n \mathbf{A}(w_{m,k}^{n,l-1}) \nabla J_l(\tilde{\mathbf{W}}^{n,l-1}) \right] \quad (15)$$

where n is the iteration index, l is the sub-iteration index, P is the projection operator onto $\theta \equiv \{w_{m,k}^{n,l} : \varepsilon \leq w_{m,k}^{n,l}(j) \leq U - \varepsilon, j=1, \dots, N\}$ with ε being a small positive number and U being an upper bound (Ahn & Fessler 2003), α_n is a relaxation parameter, and $\mathbf{A}$ is a diagonal scaling operator. For brevity we refer the reader to (Gravier et al. 2007) for more details.

In the experiments, $L = 8$ was used; the subsets were formed such that the projections in two consecutive subsets were separated as far as possible. The number of iterations used was 10.

The step size α_n was set to $\frac{1}{n+1}$ with n being the iteration index.

Appendix B: Definition of Reconstruction Accuracy Measures

5.1. Mean square error (MSE)

The MSE of the reconstructed gated dynamic images of the myocardium is computed as

$$\text{MSE} = \frac{1}{TKN} \sum_{t=1}^T \sum_{k=1}^K \|f_{t,k} - \hat{f}_{t,k}\|_{\text{ROI}}^2 \quad (16)$$

where $\hat{f}_{t,k}$, $f_{t,k}$ denote the reconstructed and reference images, respectively, ROI denotes a volume containing the entire myocardium, and N is the total number of voxels in the ROI.

5.2. Bias-variance analysis

For a given reference image f we use $\bar{f}_{\text{ROI}}$ to denote its average intensity in a specified ROI, i.e.,

$$\bar{f}_{\text{ROI}} = \frac{1}{M} \sum_{i \in \text{ROI}} f(i) \quad (17)$$

where M is the total number of pixels within the ROI.

Let $\hat{f}^{(q)}$, $q = 1, \dots, Q$, denote the estimates of f from Q different noise realizations. Then the mean intensity of the ROI is estimated as follows:

$$\hat{\mu} = \frac{1}{Q} \sum_{q=1}^Q \hat{f}_{ROI}^{(q)} \quad (18)$$

The bias and standard deviation (std) of the estimator in (18) are then respectively estimated (in relative percentage) as

$$\text{bias} = \frac{|\bar{f}_{ROI} - \hat{\mu}|}{\bar{f}_{ROI}} \times 100\% \quad (19)$$

$$\text{std} = \frac{\sqrt{\frac{1}{Q-1} \sum_{q=1}^Q (\hat{f}_{ROI}^{(q)} - \hat{\mu})^2}}{\bar{f}_{ROI}} \times 100\% \quad (20)$$

In our experiments, a total of 30 noise realizations were used for generating the bias-standard deviation plots.

5.3. Contrast-to-noise ratio (CNR)

For a defect, the average and peak CNR values are computed as follows:

$$\overline{\text{CNR}} = \frac{1}{T} \sum_{t=1}^T \frac{|m_n(t) - m_d(t)|^2}{(\sigma_n^2(t) + \sigma_d^2(t))/2} \quad (21)$$

$$\text{CNR}_{\max} = \max_t \frac{|m_n(t) - m_d(t)|^2}{(\sigma_n^2(t) + \sigma_d^2(t))/2} \quad (22)$$

where $m_n(t)$ and $m_d(t)$ are the average values of the normal myocardium and the defect, respectively, at time t , and $\sigma_n(t)$ and $\sigma_d(t)$ denote their corresponding standard deviation values.

For each noise realization, $m_n(t)$ and $m_d(t)$ were computed from the normal and defect ROIs as in Fig. 3; the variances $\sigma_n^2(t)$ and $\sigma_d^2(t)$ were estimated using an enlarged set of voxels surrounding each ROI for stabilization.

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Figure 1.
Time activity curves introduced for different organs.

Figure 2.
A short-axis slice of NCAT phantom for gate #1 with a simulated perfusion defect (indicated by x's) in the anterior wall of the left ventricle.

Figure 3. Different regions of interest (ROIs) used in evaluation including MSE, TAC, bias-variance analysis and CNR. Normal: “o”; defect: “x”.

(a) B-spline

(b) dEM

Figure 4. MSE results of the reconstructed myocardium ROI obtained from 30 noise realizations by B-spline and dEM.

(a) At time 1.78 min.

(b) At time 4.78 min.

(c) At time 10.03 min.

Figure 5.

Bias-standard deviation plots of the normal ROI obtained with 30 noise realizations at three different time points by B-spline 5D and dEM 5D. For each method, the plots are given for different temporal parameter values: 1) B-spline 5D, $\beta_\tau = 0$ (MAP-S), $\beta_\tau = 2 \times 10^{-4}$ (5D-I), $\beta_\tau = 1 \times 10^{-3}$ (5D-II); 2) dEM 5D, $\beta_\tau = 0$ (MAP-S), $\beta_\tau = 1 \times 10^{-6}$ (5D-I), $\beta_\tau = 3 \times 10^{-5}$ (5D-II). Each curve was obtained by increasing the spatial parameter over its operating range (upper left to lower right).

(a) B-spline 5D

(a) dEM 5D

Figure 6.
Time activity curves of normal ROI and defect ROI obtained by B-spline and dEM.

Figure 7.

Center location of the CHO detector for the defect shown at different time points: 1.78 min, 5.91 min and 11.91 min. Note that the visibility of the defect is time-varying.

Figure 8.
CHO detection Az results obtained from the dynamic axis of the 5D images over the imaging period by B-spline and dEM.

Figure 9.

Reconstructed dynamic images by different reconstruction methods: (1) Ideal: EM reconstruction from 360° , noiseless projection data; (2) B-spline 5D: B-spline MAP with both spatial and temporal smoothing ($\beta_s = 5 \times 10^{-5}$, $\beta_t = 1 \times 10^{-3}$); and (3) dEM 5D: dEM MAP with both spatial and temporal smoothing ($\beta_s = 2 \times 10^{-7}$, $\beta_t = 3 \times 10^{-5}$). For each approach, the ordinate represents the time post-injection, and the abscissa represents the gate number.

(a) B-spline

(b) dEM

Figure 10.

Kinetic composite parametric maps derived from the dynamic axis of the 5D images with B-spline and dEM.

Table 1

Average and peak contrast-to-noise-ratio (CNR) from three different methods: 1) B-spline 5D ($\beta_s = 5 \times 10^{-5}$, $\beta_\tau = 1 \times 10^{-3}$) and 2) dEM 5D ($\beta_s = 2 \times 10^{-7}$, $\beta_\tau = 3 \times 10^{-5}$). The mean and standard deviation (SD) were obtained from 30 noise realizations.

Methods	CNR (SD)	CNR _{max} (SD)
B-spline 5D	5.54 (1.91)	17.39 (7.00)
dEM 5D	2.86 (1.04)	10.63 (4.08)