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Adaptive anatomical preservation optimal denoising for radiation therapy daily MRI

Rapeepan Maitree,^a Gloria J. Guzman Perez-Carrillo,^{b,c} Joshua S. Shimony,^b H. Michael Gach,^{a,b,d} Anupama Chundury,^a Michael Roach,^a H. Harold Li,^a and Deshan Yang^{a,d,*}

^aWashington University School of Medicine, Department of Radiation Oncology, St. Louis, Missouri, United States

^bWashington University School of Medicine, Mallinckrodt Institute of Radiology, St. Louis, Missouri, United States

^cUniversity of Arizona, Department of Radiology, Tucson, Arizona, United States

^dWashington University School of Medicine, Department of Biomedical Engineering, St. Louis, Missouri, United States

Abstract. Low-field magnetic resonance imaging (MRI) has recently been integrated with radiation therapy systems to provide image guidance for daily cancer radiation treatments. The main benefit of the low-field strength is minimal electron return effects. The main disadvantage of low-field strength is increased image noise compared to diagnostic MRIs conducted at 1.5 T or higher. The increased image noise affects both the discernibility of soft tissues and the accuracy of further image processing tasks for both clinical and research applications, such as tumor tracking, feature analysis, image segmentation, and image registration. An innovative method, adaptive anatomical preservation optimal denoising (AAPOD), was developed for optimal image denoising, i.e., to maximally reduce noise while preserving the tissue boundaries. AAPOD employs a series of adaptive nonlocal mean (ANLM) denoising trials with increasing denoising filter strength (i.e., the block similarity filtering parameter in the ANLM algorithm), and then detects the tissue boundary losses on the differences of sequentially denoised images using a zero-crossing edge detection method. The optimal denoising filter strength per voxel is determined by identifying the denoising filter strength value at which boundary losses start to appear around the voxel. The final denoising result is generated by applying the ANLM denoising method with the optimal per-voxel denoising filter strengths. The experimental results demonstrated that AAPOD was capable of reducing noise adaptively and optimally while avoiding tissue boundary losses. AAPOD is useful for improving the quality of MRIs with low-contrast-to-noise ratios and could be applied to other medical imaging modalities, e.g., computed tomography. © 2017 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: [10.1117/1.JMI.4.3.034004](https://doi.org/10.1117/1.JMI.4.3.034004)]

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1 Introduction

The MRIdian system (Viewray, Inc., Oakwood Village, Ohio) is a radiation therapy (RT) system that integrates a 0.35-T magnetic resonance imaging (MRI) system with three multileaf collimator-equipped ⁶⁰Co radiation sources. The MRI components of the MRIdian system are designed and optimized to support image guidance for daily MRI-guided RT (MRIgRT).^{1–3}

MRIs obtained by the MRIdian system typically have more noise than images obtained on standard diagnostic MRI scanners (e.g., ≥ 1.5 T) due to the lower magnetic field strength (0.35 T).⁴ While the MRIdian image quality is adequate for RT treatment image guidance, it is not optimized for quantitative clinical and research applications including automatic organ segmentation for rapid treatment plan adaptation, evaluation of tumor response, image registration, voxel classification, radiomic image feature analysis, image features detection, and image matching.^{3,5} The MRIdian MRIs of an abdominal cancer patient are shown in the top row of Fig. 1. These images were acquired rapidly with the standard clinical image protocol: three-dimensional true fast imaging with steady-state precession (3-D TrueFISP) pulse sequence, 25 s scan, $384 \times 384 \times 144$ voxels, and a $1.5 \times 1.5 \times 3$ mm³ voxel resolution. In comparison, the

MRI images of the same patient, obtained on a clinical 1.5-T Philips Ingenia MRI, are shown in the bottom row. A two-dimensional half-Fourier acquisition single-shot turbo spin-echo (2-D HASTE) pulse sequence was used to acquire these diagnostic MRIs, separately in transverse, coronal, and sagittal planes of $320 \times 320 \times 26$ voxels and a $1.3 \times 1.3 \times 7$ mm³ voxel resolution. The total scan time was 2 min and 18 s or on average 46 s per scan.

There is a need to further improve the MRIdian image quality in order to facilitate or enable additional quantitative clinical and research applications.^{6,7} One potential solution is to apply post-processing methods such as intensity inhomogeneity correction, artifact correction, and image noise reduction. Image noise reduction by postprocessing would be useful for improving the visibility of the soft tissues, the apparent image contrast, and the general detectability of the tumor targets and the normal tissues. Typical methods of noise reduction, e.g., increasing the image acquisition time or increasing the number of signal averages, are not feasible for MRIgRT due to the clinical workflow (i.e., the types of scans performed and the machine time allocated per patient procedure) and physiological motion.

In MRI, the signal rises with the square of the field strength (B_0).⁸ The noise consists of thermal noise contributions from the

*Address all correspondence to: Deshan Yang, E-mail: yangdeshan@wustl.edu

Fig. 1 (Top) an example of a patient's 0.35-T MRIs from the MRIdian system using 3-D TrueFISP sequence (voxel size = $1.5 \times 1.5 \times 3 \text{ mm}^3$) in (a) transverse, (b) coronal, and (c) sagittal views. (Bottom) An example of patient's images from a Philips Ingenia 1.5-T MRI using a 2-D HASTE pulse sequence (voxel size = $1.3 \times 1.3 \times 7 \text{ mm}^3$) in (d) transverse, (e) coronal, and (f) sagittal views. Window level = [0,200].

receiver coils and the body and physiological noise. The thermal noise power rises with B_0 according to $B_0^{0.5}$ for receiver coils and B_0^2 for the body. For field strengths $\geq 0.3 \text{ T}$, one can assume that noise from the body dominates and SNR rises linearly with B_0 .⁹ Noise in the complex MRI k -space data is Gaussian with a zero mean prior to image reconstruction.⁸ The noise becomes Rayleigh distributed in the background regions and Rician distributed in signal regions after obtaining the image magnitude for conventional Cartesian k -space acquisitions.

Many image domain postprocessing noise reduction algorithms have been previously published. Simple methods include low-pass filtering, median filtering, moving window averaging, and total variation optimization.^{10–12} These simple methods generally reduce the soft tissue contrast and the effective spatial resolution. Prior to developing the proposed adaptive anatomical preservation optimal denoising (AAPOD) algorithm, we evaluated multiple advanced denoising algorithms that were developed to preserve the image gradient: anisotropic diffusion filters,^{13,14} wavelet-based filters,^{15–17} principal component analysis (PCA)-based,^{18,19} and nonlocal means (NLM)-based filters.^{20–26} Even with these state-of-the-art methods, the denoising results were often suboptimal, as in either inadequate noise reduction or significant loss of anatomical structure information.^{15,21,22,27,28}

To reduce image noise while preserving structural information, both the image noise and the anatomical information in the acquired image should be considered together.^{29–31} Prior algorithms adjusted the denoising filter strength according to the measured local structural information, the percentage of the maximum intensity level, the dominance of wavelets, and principle components, or visual assessments.^{20,21,26,31} In the wavelet-NLM filter algorithm,¹⁵ the denoising parameter is

adapted over the different spatial frequency resolutions of the image. In the PCA-NLM algorithm,³² the PCA is computed globally once and a lower-dimensional subspace is used to replace the Gaussian-weighted Euclidean distance that is computed between the neighboring blocks in the original NLM algorithm. Consequently, in the PCA-NLM-based algorithm, the denoising parameter depends on the dimensionality of the PCA subspace. In a more recent MRI denoising method using nonlocal PCA,³¹ the noisy image is first filtered using nonlocal PCA by automatically estimating the local noise level in the image before the filtered image is used as a guide in the rotationally invariant NLM [prefiltered rotationally invariant nonlocal means (PRI-NLM)] filter.

Figure 2 shows the denoising results of two advanced denoising algorithms, 3-D adaptive block matching (ABM4D)^{27,28} and 3-D PRI-NLM²¹ on MRIdian 3-D MRIs. These two algorithms were optimized from previous NLM algorithms to preserve image details adaptively. While the localization and heterogeneity of image noise distribution are considered in these adaptive denoising algorithms, the preservation of the structural information (e.g., tissue boundaries) is still inadequate. Three denoising filter strengths were used in this example to demonstrate that, without fine-tuning the denoising parameters, the results of these most advanced adaptive denoising algorithms can be suboptimal. For the ABM4D algorithm, the three levels were implemented by multiplying the estimated image noise by 50%, 100%, and 200%. Insufficient noise reduction is observed at the lower denoising filter strengths [Figs. 2(a) and 2(d)]. Oversmoothing is observed at the high denoising filter strengths [Figs. 2(c) and 2(f)]. Uneven denoising is present with moderate denoising strengths [Figs. 2(d) and 2(e)]. Losses of anatomical structure details and insufficient noise reductions are observed

Fig. 2 The denoising results using the algorithms (left) 3-D PRI-NLM and (right) 3-D ABM4D. The denoised image window level = $[0,200]$. The difference image window level = $[-20,20]$.

in both the denoised images and the difference images (i.e., the difference between the denoised image and the original image) when compared to the original MRIs.

In this study, we developed a denoising algorithm, AAPOD, to improve the preservation of the image structural information, i.e., tissue boundaries, during image denoising. Tissue boundaries in the study refer to the 3-D interfaces between different anatomical structures (organs, vessels, bones, tumors, and etc.) in the *in vivo* images. Such tissue boundaries are important for many different clinical applications, e.g., organ and tumor target contouring, patient alignment for treatment setup, and automatic image segmentation and registration. Losses or degradation of tissue boundaries negatively affect the accuracy of the respective clinical applications. In AAPOD, we incorporated a direct assessment of tissue boundary losses into the denoising process. AAPOD adaptively fine-tunes the denoising filter strengths according to both local noise statistics and local tissue boundary information to obtain maximal noise reduction and minimal tissue boundary losses.

AAPOD is similar to prior adaptive denoising algorithms.^{22,26,28,31} However, AAPOD uses a more direct approach to determine the optimal denoising filter strength as the maximal value without causing losses in structural information. The most important innovations in AAPOD are that it:

(1) directly assesses the tissue boundary losses using edge detection on the “difference of the sequentially denoised” (DoSD) images and (2) adapts the denoising filter strength by considering both local noise variations and the local tissue boundary losses.

2 Materials and Methods

2.1 Images

T_1 - and T_2 -weighted MRIs of human brains with multiple sclerosis lesions were obtained from the BrainWeb database^{33,34} and used to quantitatively evaluate the performance of AAPOD and well-established adaptive denoising methods. The MRIs had 1-mm-thick slices, with added noise (3%, 5%, and 7%). The noise level represents the percent ratio of the standard deviation of the Gaussian noise added to the complex image data versus the brightest tissue signal in the magnitude image.

For further quantitative assessment, a fresh cadaver swine head was scanned 34 times on the 0.35-T MRIdian system using 3-D TrueFISP MRI scan sequence (TE = 1.6 ms, TR = 3.8 ms, $1.5 \times 1.5 \times 3$ mm³ voxel resolution, rBW = 385 Hz/pixel, 6/8 partial Fourier for both phase and slice directions, GRAPPA 2, flip angle = 60 deg, asymmetric echo, and average scan time = 17 to 25 s). The minimal noise semiground-truth image was

computed by averaging the 34 scans. For each individual scan, a noise map was calculated as the difference between the individual scan and the averaged scan. The overall noise variance map was calculated as the standard deviation of the 34 noise values at each voxel position.

In addition, 40 MRIdian patient MRIs and 20 CT patient images were denoised using the proposed AAPOD methods. The denoising results were visually assessed and ranked by two experienced radiologists (G. G. and J. S.) and one MRI medical physicist (M. G.). The 40 patient MRIdian MRIs were retrospectively obtained from the previous daily patient treatment MRIdian MRI scans. Patient images were selected to cover major anatomical sites from brain to pelvis. The 20 CT patient images were retrospectively obtained from the previous patient CT scans for the radiation treatment planning purposes. Abdomen and pelvis CT images were included in this study because these images are noisier than CT images of other body positions due to the use of 120 kVp required by the clinical protocol.

Finally, T_1 -weighted MRIs of an American College of Radiology (ACR) phantom obtained on the MRIdian system (TE = 20 ms, TR = 500 ms, spin-echo sequence, and rBW = 78 Hz/pixel) were used to test the effects of denoising on low-contrast detectability.

2.2 Basics of Nonlocal Means-Based Denoising

AAPOD is based on the existing adaptive nonlocal-means (ANLM) algorithm.²² All NLM algorithms perform denoising by computing the intensity, for each voxel, as the weighted mean of similar voxels in close proximity. In comparison, the local mean denoising algorithms, such as Gaussian smoothing and moving window averaging, compute the distance-weighted mean intensity of the surrounding voxels. The NLM denoising algorithms perform significantly better than local mean algorithms by factoring the neighborhood similarity into the relative weighting in the mean operation. However, the NLM algorithms also carry significantly more computational costs.^{25,30,35}

In the standard NLM method,²⁵ the denoised voxel's intensity $\hat{u}(x)$ is calculated as the weighted average of all voxels' intensities in a search volume V_i that is near the voxel x

$$\hat{u}(x_i) = \sum_{x_j \in V_i} w(x_i, x_j) u(x_j), \quad (1)$$

where $u(x_i)$ and $u(x_j)$ are the intensity of voxel x_i and voxel x_j , $w(x_i, x_j)$ is the weighting coefficient assigned to $u(x_j)$, determined by the similarity between the local neighborhood blocks B_i and B_j centered on voxels x_i and x_j , and

$$w(x_i, x_j) = \frac{1}{Z_i} e^{-\frac{\|B_i - B_j\|_2^2}{h^2}}, \quad (2)$$

where $\|B_i - B_j\|_2^2$ is the Gaussian-weighted Euclidean distance between the neighboring blocks B_i and B_j , h is the filter strength parameter that acts as a denoising parameter controlling the decay of the exponential function, and Z_i is the normalization constant to ensure

$$\sum_{x_j \in V_i} w(x_i, x_j) = 1. \quad (3)$$

h and the sizes of V and B are user defined. The standard NLM algorithm uses a global constant h value on all voxels.

However, regions in the image usually have different intensities and noise levels. Therefore, each region requires a different optimal denoising filter strength h , which could be defined as the highest h value that does yield tissue boundary loss in the region. The denoising method becomes adaptive, i.e., the adaptive NLM (ANLM), when an NLM method adapts its h parameter values based on the characteristics of the image.^{22,26,29,36,37}

Previous studies have suggested that the optimal values for h could be selected to be proportional to the noise variation.^{22,25} For an image with an unknown true noise variation, the noise level, $\sigma(x_i)$, at voxel x_i , could be estimated by computing the minimal Euclidean distance of the weighted average of all blocks neighboring the voxel x_i

$$\sigma(x_i) = \sqrt{\frac{\min(E\|B_i - B_j\|)}{2}}. \quad (4)$$

Using the noise variation to infer h still does not guarantee optimal denoising results. Figure 3 demonstrates the denoising result on the swine head dataset for which the true noise variance map was computed from 34 repeated scans. In this example, the denoising was not adequate when the true noise variance map was used as the denoising filter strength h in the ANLM [Figs. 4(b) and 4(e)]. Doubling the true noise variance magnitude produced a better noise reduction result [Figs. 4(c) and 4(f)]. However, tissue boundary losses in the denoised images were observed.

2.3 Determine the Optimal Denoising Strength Parameter

From the preliminary results shown in Fig. 3, it appears that an optimal value for the denoising filter strength h provides an optimal denoising result. Optimal denoising removes the noise entirely without degrading the true image. For *in vivo* images, the ground-truth is unknown and ideal optimal denoising is unobtainable. In this study, we refer to optimal denoising as the ANLM using the optimal h values, i.e., the maximal h values before the tissue boundary losses start to appear in the denoised image.

Figure 4 shows a series of denoising results by setting the filter strength parameter h to the noise variance map $\sigma(x)$ multiplied by a series of incremental values (from 0.4 to 1.3 in a step of 0.15). There is an increasing smoothness in the denoised images [Fig. 4(a)], suggesting gradual losses of tissue boundaries. However, it is very difficult to tell the tissue boundary deterioration directly and quantitatively in the denoised image because tissue structures are still very visible. It is also difficult to tell the lost tissue boundaries in the difference images (the difference between the denoised images and the original noisy images), shown in Fig. 4(b), because the difference images contain the removed noise as well as the lost tissue boundaries.

The DoSD images are shown in Fig. 4(c). It is much easier to identify the tissue boundary in the DoSD images. The DoSD images contain only the incrementally removed noise and the incremental tissue boundary losses between two images denoised using the incremental denoising filter strengths. The DoSD images contain only the additional noise removed at the increased h value in the regions where image noise is not yet maximally removed, i.e., $h(x) < \hat{h}(x)$ where $\hat{h}(x)$ is the hypothetical optimal denoising filter strength map. Such cases can be observed in the first two DoSD images in the series.

Fig. 3 Demonstration of using the true noise variance as the denoising filter strength parameter h in the ANLM algorithm on 0.35-T MRIdian MRIs of the swine head. In the top row, (a) the noisy images, (b) and (c) the denoised images, and (d) the ground-truth image (by averaging the 34 scans), window level = $[-150, 350]$. In the bottom row, (e) and (f) the removed noise (difference) images and (g) the truth noise image, window level = $[-20, 20]$.

Fig. 4 Demonstration of denoising using a progressively increasing value for the filter strength parameter. Tissue boundary losses are not evident in the denoised images in (a), or in the difference images in (b), but are very evident in the DoSD images in (c).

The DoSD images contain only the incremental tissue boundary losses in the regions where image noise is maximally removed, i.e., $h(x) > \hat{h}(x)$, because no additional noise is removed at the increased h values. Such cases can be observed in the last three DoSD images in the series. Generally, tissue boundary losses start to appear in the DoSD images when the filter strength parameter h goes from a value below $\hat{h}$ to a second value above $\hat{h}$. In this example, the tissue boundary losses start to appear in the third DoSD image which was obtained with $h(x) = 0.75 \times \sigma(x)$, suggesting that $\hat{h}(x) \in [0.6, 0.75] \times \sigma(x)$.

σ , h , and $\hat{h}$ are all dependent on position. Henceforth, we will omit the voxel coordinate variable x in the following equations and notations.

It is possible to detect the lost tissue boundaries in each DoSD image in order to determine the value $\hat{h}$ since the tissue boundary losses start to appear in a DoSD image at $h > \hat{h}$. The optimal denoising is achieved by applying the ANLM method using the $\hat{h}$ map after the $\hat{h}$ map is determined for the entire image. A theoretical analysis of the DoSD images and the tissue boundary losses is presented in the [Appendix](#).

2.4 Adaptive Anatomical Preservation Optimal Denoising

Following the observations presented in the previous sections, we have developed a new algorithm, AAPOD, that automatically determines the optimal denoising strength map h in order to accomplish the maximal noise reduction while avoiding tissue boundary losses. As illustrated in the AAPOD workflow (Fig. 5), an image is denoised in six major steps with AAPOD.

Step 1 The initial filter strength map $\sigma(x_i)$ is computed based on the estimated noise statistics of the original image [Eq. (4)].

Step 2 A series of denoised images are computed by denoising the image using the NLM method with the initial filter strength map $\sigma(x_i)$, scaled by a series of multiplication factors. For denoising step n , the denoising filter strength map is generated as

$$\sigma_n(x_i) = a_n \cdot \sigma(x_i), \quad n = (1:N), \quad (5)$$

where a_n is a set of multiplication factors, N is the total number of filter strength maps, and $\sigma(x_i)$ is the initial filter strength map, i.e., the noise variance map estimated using Eq. (4) at voxel x_i .

Step 3 The sequence of DoSD images computed as the difference of each pair of adjacent denoised images in the denoised image series

$$D_n(x_i) = \hat{u}(x_i)|(h = \sigma_{n+1}) - \hat{u}(x_i)|(h = \sigma_n), \quad (6)$$

$$n = (1:N - 1),$$

where $D_n(x_i)$ is the n 'th DoSD image, and $\hat{u}(x_i)|(h = \sigma_n)$ and $\hat{u}(x_i)|(h = \sigma_{n+1})$ are the denoising results using ANLM with the denoising filter strength parameter $h = \sigma_n(x_i)$ and $\sigma_{n+1}(x_i)$. Note that the total number of DoSD images is $N - 1$.

Step 4 The incrementally lost tissue boundaries are detected in the DoSD images using a zero-crossing edge detection algorithm.³⁸ As explained in the appendix, the DoSD images at $h > \hat{h}$ are approximately the differences of Gaussian (DOG) of the optimal denoised image. Edges in such DOG images appear as zero-crossing,³⁹ therefore, a zero-crossing detector was selected as the edge detector for this step.

Step 5 The optimal denoising strength $\hat{h}$ for each voxel is defined such that, in the initial denoising sequence, (1) there is no tissue boundary loss at the voxel in

the denoised image at the optimal h value, and (2) there is a tissue boundary loss detected in the denoised image at a larger value of h . $\hat{h}$ is computed as

$$\hat{h}(x_i) = \sigma_{n'}(x_i)|[n' = n'_{\text{opt}}(x_i)], \quad (7)$$

where $\hat{h}(x_i)$ is the optimal map of the denoising parameter for the original noisy image $u(x_i)$. $n'_{\text{opt}}(x_i)$ is the optimal denoising filter strength at the voxel x_i , computed by finding the maximal n in $\sigma_n(x_i)$ that will not cause the loss of the tissue boundary at the voxel x_i

$$n'_{\text{opt}}(x_i) = \max(n) | E_n(x_i) = 0, \quad n = (1:N - 1), \quad (8)$$

where $E_n(x_i)$ is the tissue boundary loss detected in the n 'th DoSD image $D_n(x_i)$, and $E_n(x_i) = 1$ stands for a tissue boundary loss detected in $D_n(x_i)$ at the voxel x_i . When $E_n(x_i) = 0$, there is no tissue boundary loss at x_i .

Step 6 The final denoising image is computed by denoising the original noisy image using Eqs. (1) and (2) with the final denoising parameter map $\hat{h}(x_i)$.

2.5 AAPOD Parameters and Implementation Details

The main AAPOD algorithm [Eqs. (5)–(8)] was implemented in MATLAB version 2015a (Mathworks, Massachusetts). The noise variance map estimation [Eq. (4)] and the 3-D ANLM functions [Eqs. (1)–(3)] were implemented in C++.

The parameters used by AAPOD are listed in Table 1. The values were learned empirically according to the preliminary results with the daily MRIdian MRIs. For example, $N = 7$ was selected as a compromise between the total computation cost and the denoising image quality. The filter strength parameter minimal $a_n = 0.4$ was selected as the maximal value prior to tissue boundaries starting to appear. The maximal value $a_n = 1.3$ was selected so that any greater a_n value removed only tissue boundaries. We also empirically selected the search volume V size = $5 \times 5 \times 5$ voxels, and the neighborhood block B size = $3 \times 3 \times 3$ voxels. We found that increasing the sizes of the search volume and the neighborhood block significantly increased the computation cost, but led to only marginal increases in the visual and quantitative quality of the denoised image.

We used the zero-crossing detector in the MATLAB® image processing toolbox for edge detection. A DoSD image contains the incrementally reduced noise in the regions for $h < \hat{h}$. The

Fig. 5 The overall workflow of the proposed AAPOD algorithm. There are six major steps and two optional side steps. The side steps are shown as the dashed-lines.

Table 1 Parameters used by AAPOD.

#	Parameters	Values
1	Number of initial denoising steps N	7
2	Initial denoising scale factors α_n	[0.4 0.55 0.6 0.85 1.0 1.15 1.3]
3	NLM search volume V	$5 \times 5 \times 5$ voxels
4	NLM neighborhood block size B	$3 \times 3 \times 3$ voxels
5	Zero-crossing edge detection threshold	$3 \times 10^{-3} \times \text{maximal voxel intensity}$
6	False edge rejection length N_E	10

zero-crossing edge detector would also detect noise in the DoSD images as false tissue edges. False tissue edges, i.e., noise voxels, are separated and contain only a single or a few voxels compared to real tissue edges that contain many connected voxels. In addition, the edges detected in the last DoSD image (of highest h values and $h > \hat{h}$) are significantly more stable than the edges detected at smaller h values ($h < \hat{h}$) because the last DoSD image contains the least noise. Following these two observations, an extra step was implemented to reject the false edges. An edge voxel must meet two conditions or it will be rejected as a false edge voxel: (1) the voxel is on an edge detected in the last DoSD image and (2) the number of connected edge voxels $> N_E$. We use $N_E = 10$ in this study. Figure 6 shows examples of the detected tissue boundaries in the DoSD images that are shown in Fig. 5(c).

A simple morphologic filter was applied on the results of the edge detection in order to expand the detected edge map by 2 voxels and to avoid tissue boundary losses in the final denoising image. The final denoising filter strength map $\hat{h}$ was further smoothed using a Gaussian low-pass filter and a Gaussian kernel size of 2 voxels to ensure the overall continuous smoothness. Finally, the smoothed $\hat{h}$ was applied in the final denoising computation.

The default parameters provided in Table 1 worked well for most MRIdian MRIs that we tested in the preliminary studies. However, clinical tolerance of certain tissue edge losses is often patient-specific for patient and the edge detector tolerance is

sensitive to the imaging modality, e.g., MRI and CT, and the anatomical site. We have, therefore, implemented two side steps in the AAPOD workflow (Fig. 5). In step 1(b), the optimal settings for AAPOD were selected for the target imaging modality. In step 4(b), which is optional, a user can visually check the detected edges in the DoSD images and determine if the edge detection sensitivity shall be adjusted by adjusting the edge detection threshold parameter. If the user decides to adjust the edge detection sensitivity, steps 4 to 6 (Fig. 5) will be repeated with the new parameter.

2.6 Image Quality Evaluation

The mean squared error (MSE) of image intensity, the mean absolute error (MAE) of the 3-D image gradient magnitude,⁴⁰ and the structural similarity index (SSIM)⁴¹ were applied on the denoising results of the 0.35-T swine head dataset and the BrainWeb datasets. The average scan of the 34 scans for the swine head and the ground-truth images for the BrainWeb datasets were applied as the reference to quantitatively assess the denoising algorithms. MSE measures the level of the image intensity error between the ground-truth and the denoising results. MAE measures the accuracy of the denoised image's gradient magnitude, i.e., the losses of the image structural information.

$$\text{MAE} = \frac{1}{N} \sum_{i=1}^N |GT_i - GD_i|, \quad (9)$$

where N is the total number of voxels in the image, GT_i is the image gradient magnitude at a voxel i of the ground-truth image, and GD_i is the image gradient magnitude at the voxel i of the denoised image.

In addition, a subjective assessment was performed by two experienced radiologists (G. G. and J. S.) and one MRI medical physicist (M. G.) using 60 sets of *in vivo* data (40 MRIdian MRI cases and 20 CT cases) and the denoised images from the AAPOD algorithm, 3-D wavelet subbands mixing algorithm,¹⁵ and 3-D adaptive block matching (ABM4D) algorithm.

3 Results

Performance of the zero-crossing edge detector was evaluated using a XCAT2 digital phantom.⁴² The example in Fig. 7

Fig. 6 The detected tissue boundary losses in the DoSD images that are shown in Fig. 5(c). Window level = [0, 1].

Fig. 7 Demonstration of the zero-crossing edge detection on the XCAT2 digital phantom image. (a) An axial slice of XCAT2 image in the upper abdomen. (b) The detected edges overlaid on the same axial slice. Window level = $[-200\ 100]$.

Fig. 8 Examples of the T_1 -weighted MRI images from the BrainWeb database and the denoising results. Window level = $[0, 1200]$. ABM4D, adaptive block matching; PRI-NLM, prefiltered rotationally invariant NLMs; wavelet, wavelet subbands mixing.

shows that the edge detector was capable of detecting all tissue edges on the XCAT2 digital phantom image, including the edges of minor intensity differences between the liver and the right kidney. The edge positional accuracy was visually estimated as ≤ 1 pixel.

Figure 8 shows the denoising results from three denoising algorithms of T_1 -weighted MRIs acquired from the BrainWeb database with added noise. ABM4D, PRI-NLM, and wavelet subbands mixing algorithms were included in this comparison because they are among the most recent and advanced adaptive methods, and are specially designed to preserve the image features. Since the PRI-NLM and the wavelet subbands methods are not fully automatic, the authors manually optimized the parameters to obtain the best results. As one can see visually for the remaining image noises in the denoising results, both AAPOD and the ABM4D algorithms performed satisfactorily and generated significantly better results than the results of the PRI-NLM and the wavelet subbands algorithms.

Table 2 displays the MSEs of the image intensity and the MAEs of image gradient measurements on the denoised T_1 - and T_2 -weighted BrainWeb MRIs. The MSEs of image intensity measurements suggested that AAPOD performed the best. The MAEs of image gradient magnitude measurements indicated that AAPOD outperformed the other three algorithms in preserving the image gradients at all noise-adding levels. AAPOD and ABM4D algorithms were the top two performers in the SSIM measurements.

Figure 9 and Table 3 illustrate a comparison of the denoising results on the swine head dataset using six 3-D advanced and adaptive denoising methods: (1) NLM, (2) ANLM (with the true noise variance as the denoising parameter h), (3) wavelet subbands Mixing, (4) PRI-NLM, (5) ABM4D, and (6) AAPOD. The NLM, ANLM, wavelet, and PRI-NLM methods are not fully automatic and the best results with these methods were selected by manual optimization of each algorithm's parameters and visual assessments. ABM4D is fully automatic and determines its denoising filter strength by automatically estimating the image noise.

Comparing the amount of the removed noise and the structural information losses in the difference images [Figs. 9(d)–8(i) bottom] and in the ground-truth noise image [Fig. 9(c)], one can see that AAPOD satisfactorily removed noise while avoiding tissue boundary losses. Furthermore, according to Table 3, AAPOD produced the best results compared to the other denoising algorithms, yielding the smallest MSE and MAE values. Additionally, denoising using AAPOD is approximately equivalent to reducing the scan time by 50% since the MSE and MAE values of the AAPOD results were very close to the values of the two averaged scans.

The subjective assessments on *in vivo* images from the MRIdian system are shown in Figs. 10 and 11. Improvements in the appearance of soft tissues and their boundaries in the denoised images are evident. The difference images demonstrate that AAPOD can significantly reduce the image noise without losses of anatomical structures.

Table 4 summarizes the subjective assessments of the images by a panel of two radiologists (G. G. and J. S.) and one MRI medical physicist (M. G.). The subjective assessments were performed on the 40 sets of the original MRIdian MR images, and the denoised images obtained using the AAPOD, wavelet, and ABM4D algorithms. Each image was scored from 0 to 3 by the three radiologists where 0 = worst, unacceptable, 1 = worse than acceptable, barely adequate to support clinical decision, 2 = acceptable, adequate to support clinical decision, and 3 = more than adequate and visually praiseworthy. Based on a pairwise *t*-test, the *p* values (versus the original), all less than 0.05, suggest that the denoised images by any denoising methods are statistically significantly better than the original images. However, the *p* values (versus AAPOD) suggest that the AAPOD results are not significantly better than the results obtained by the wavelet or the ABM4D methods, even though the AAPOD average scores are the highest.

AAPOD was also tested on CT images, as shown in Fig. 12. The panel of three experts confirmed the AAPOD denoising performance on CT images in the subjective assessment (Table 5). AAPOD received the highest average score with the lowest standard deviation. Note that the original images received

Table 2 The measured MSEs of image intensity, MAEs of gradient magnitude and SSIM (structural similarity) in the denoising results on the BrainWeb MRIs with three different noise levels added (3%, 5%, and 7% of the maximal intensity).

MRI	Noise	MSE of image intensity					MAE of gradient magnitude					SSIM				
		N ^a	W ^b	P ^c	A ^d	AA ^e	N ^a	W ^b	P ^c	A ^d	AA ^e	N ^a	W ^b	P ^c	A ^d	AA ^e
T_1	3%	460	150	127	118	90	94	72	62	75	63	0.86	0.90	0.90	0.94	0.93
	5%	1238	443	404	206	179	157	122	110	109	94	0.78	0.83	0.82	0.92	0.90
	7%	2357	940	901	293	270	222	174	161	138	123	0.70	0.76	0.75	0.90	0.88
T_2	3%	1144	544	443	400	229	178	162	112	159	104	0.81	0.84	0.84	0.91	0.91
	5%	2817	1510	1327	942	458	312	294	191	279	161	0.69	0.74	0.74	0.86	0.87
	7%	4950	2573	2677	1263	909	387	355	267	325	203	0.60	0.65	0.65	0.83	0.79

^aNoisy image.

^bWavelet.

^cPRI-NLM.

^dABM4D.

^eAAPOD.

Fig. 9 Comparison of noise reduction results on the 0.35-T swine head MRIs. (Top) (a) Original noisy image, (b) ground-truth image, (c) true noise image (the bright areas are caused by heterogeneity of the MRI intensity, i.e., RF signal variation during image acquisition); (center) (d–i) denoised images: window level = $[-150,350]$; (bottom) (d–i) difference images: window level = $[-20,20]$. The voxels outside the swine head were excluded from the difference images.

Table 3 The measured MSEs of image intensity, MAEs of gradient magnitude, and SSIM on the swine head denoised images (Fig. 9) and on the average of repetitive scans of the swine head. The voxels outside the swine head were excluded from the measurements.

Quality index	Noisy image	NLM	ANLM	Wavelet	PRI-NLM	ABM4D	Mean of 2 scans	Mean of 3 scans	Mean of 4 scans	AAPOD
MSE	47.76	16.67	12.88	14.29	14.81	12.97	12.20	8.17	6.34	12.28
MAE	26.32	23.19	22.77	22.73	22.71	21.48	18.85	15.10	13.57	21.85
SSIM	0.867	0.909	0.921	0.925	0.920	0.925	0.920	0.939	0.951	0.929

Fig. 10 AAPOD denoising results of the MRIdian MRI of human abdomen. (a) A transverse slice from the original noisy image, (b) the AAPOD denoised image, and (c) the difference image. Window level = $[0,200]$ for (a, b), window level = $[-20,20]$ for (c). This MRI was obtained using the clinical standard quality 3-D TrueFISP scan sequence.

a score as low as 0, whereas the AAPOD results received no score of 0. Based on a pairwise t -test, the p values (versus the original) suggest that AAPOD performed significantly better than the wavelet method. However, the results of AAPOD were

not significantly better than the original images or the ABM4D results.

The denoising results of the T_1 -weighted image of an ACR MRI phantom are shown in Fig. 13. One can see the significant

Fig. 11 AAPOD denoising results on a 0.35-T MRIdian brain MRI in the transverse, sagittal, and coronal views. (a) The original noisy image and (b) the denoised images with window level = $[-50, 450]$. (c) The difference images are with window level = $[-50, 50]$.

Table 4 Subjective assessment by a panel of three experts on 40 sets of *in vivo* images. Each set contains the original MRIdian 0.35-T MRIs and the denoised image results obtained from AAPOD, wavelet, and ABM4D algorithms. The p -values (versus AAPOD) were computed using pairwise t -tests between the scores of the images in the AAPOD group and the scores of the images in the other groups. The p -values (versus the original) were computed between the scores of the original images and the scores of the images in the other groups.

MRI 0.35 T (40 cases from MRIdian system)	Original	Wavelet	ABM4D	AAPOD
Average score (0 to 3)	1.375	1.675	1.675	1.808
Standard deviation	0.851	0.779	0.747	0.748
Lowest/highest score received	0/3	0/3	0/3	0/3
p -value (versus AAPOD)	0.004	0.177	0.168	—
p -value (versus the original)	—	0.005	0.004	0.004

noise reduction in the AAPOD denoising result, without a loss of visibility of small and low-contrast objects.

4 Discussion

The most important limitations with AAPOD are the added complexity, a higher computation cost, and the dependency on the robustness of the edge detection method. AAPOD is more complex because it uses a combination of noise estimation, multiple iterations of initial denoising, and an edge detection method. Unlike other adaptive denoising algorithms,

AAPOD directly detects the losses of tissue boundaries in the denoised images and sequentially prevents such losses in the final denoised image by optimizing the denoising filter strength parameter locally. Optimizing the final h map in AAPOD strongly depends on the robustness and accuracy of the edge detection method applied to detect the tissue boundary losses in the sequential DoSD images.

Theoretically, AAPOD could optimally reduce image noise and avoid any losses of tissue boundaries using a perfect edge detector and an initial denoising sequence employed at very fine levels. However, a perfect edge detector does not exist so we chose the zero-crossing edge detector. The zero-crossing edge detection results are relatively sensitive to the threshold parameter. Since the edge detection is a relatively independent component in AAPOD, the zero-crossing edge detector could be replaced with better methods or adapted to the image modality and the anatomical sites.

Additional adjustments could improve the computational efficiency in AAPOD. The average computation time of AAPOD running on a Windows PC with an Intel i7 CPU at 3.60 GHz, 16 GB RAM was 19.45 s for an MRI with a matrix size of $217 \times 181 \times 11$. In the standard NLM computation, used by AAPOD in the initial denoising, two of the major computation costs were: (1) gathering the neighborhood block information and (2) computing the similarity of the neighborhood blocks. If M is the number of neighborhood blocks, Q is the total number of voxels in the whole image, K is the total number of voxels in each neighborhood block, and N is the number of initial denoising sequence, computing each voxel in each neighborhood block in the initial denoising would cost $M \times Q \times K \times N$. The neighborhood block information can be computed once and stored to avoid repetitive computation.

Fig. 12 The AAPOD denoising results on a CT image. (a) The original image and (b) the denoised image, window level = [650,1350], and (c) the difference image, window level = [-50,50].

Table 5 Subjective assessment by three experienced radiologists on human CT images and the denoised image results obtained from AAPOD, wavelet, and ABM4D denoising algorithms. The p -values (versus AAPOD) were computed using pairwise t -tests between the scores of the images in the AAPOD group and the scores of the images in the other groups. The p -values (versus the original) were computed between the scores of the original images and the scores of the images in the other groups.

CT (10 cases)	Original	Wavelet	ABM4D	AAPOD
Average score (0 to 3)	1.733	1.550	1.767	1.933
Standard deviation	0.899	0.699	0.810	0.82
Lowest/highest score received	0/3	1/3	1/3	1/3
p -values (versus AAPOD)	0.205	0.007	0.265	—
p -values (versus the original)	—	0.215	0.831	0.205

In addition, a linear interpolation among the already computed ANLM results may also reduce the computational burden instead of computing a new ANLM in each initial denoising sequence. Instead of using the noise estimation, using a series of constant values to initialize the h maps is an alternative option because the final optimal h map is determined via the initial denoising sequence and detection of tissue boundary losses.

AAPOD was developed to process the 0.35-T MRIs obtained on the MRIdian system. It was also useful on CT images and MRIs obtained at higher magnetic field strengths. The full impact of the AAPOD on clinical applications and image processing, i.e., fully automatic segmentation and quantitative analysis of anatomical structures, is not addressed herein and will be investigated in future studies. Likewise, additional studies should explore the possibilities of adapting the proposed AAPOD method for other denoising algorithms, especially the detection of boundary losses in the DoSD images.

Fig. 13 (a) A high quality T_1 -weighted scan of ACR MRI phantom low-contrast detectability slice, (b) a T_1 -weighted noisy image of the phantom, (c) the denoised image by ANLM, (d) the denoised image by AAPOD, and (e) the regions of interest. All images: window level = [500,1500].

5 Conclusion

A medical image denoising algorithm, AAPOD, was developed in this study. It was designed to be an automatic process that adapts its denoising parameter values per image voxel in order to accomplish optimal noise reduction without losses of anatomical structural information. Avoidance of tissue boundary losses was accomplished by the direct detection of tissue boundary losses in the DoSD images. AAPOD was beneficial for processing noisy MRI and CT images used in RT.

Appendix: Theoretical Analysis of the DoSD Images

The NLM denoising filter is nonlinear. It is difficult to describe the denoising effects precisely as a function of the filter strength parameter h because the denoising results are also dependent on the image intensities of the neighboring voxels. However, to explain how the tissue boundary losses are visible in the DoSD images shown in Fig. 4(c), the NLM denoising result $\tilde{I}$ as a function of h can be roughly approximated as

$$\tilde{I}(h) = \begin{cases} (1-\alpha)I + \alpha\hat{I} & 0 \leq h \leq \hat{h}, \alpha = h/\hat{h} \\ g(\sigma_h) \otimes \hat{I} & \hat{h} < h < \infty, \sigma_h = (h - \hat{h})/\hat{h} \end{cases} \quad (10)$$

where I and $\hat{I}$ are the original noisy image and the hypothetical optimal denoised image, respectively, $\hat{h}$ is the optimal filter strength map, g is the Gaussian smoothing kernel with a window size σ_h , and $\otimes$ is the convolution operator.

Equation (10) suggests that the denoising result $\tilde{I}(h) = I \rightarrow \hat{I} \rightarrow \tilde{I}$ as $h = 0 \rightarrow \hat{h} \rightarrow \infty$. There is an incremental noise reduction but no tissue boundary losses at $h = 0 \rightarrow \hat{h}$. However, tissue boundary losses start to appear at $h = \hat{h}$ and increase as $h = \hat{h} \rightarrow \infty$.

For $h > \hat{h}$, a DoSD image is

$$\text{DoSD}(h_1, h_2) = \tilde{I}(h_1) - \tilde{I}(h_2) = [g(\sigma_{h_1}) - g(\sigma_{h_2})] \otimes \hat{I}. \quad (11)$$

The DoSD image is therefore approximately the DOG of $\hat{I}$. Since a DOG filter enhances the edges in the image, a DoSD image contains the incremental tissue boundary losses of $\hat{I}$ as $h > \hat{h}$.

Disclosures

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Rapeepan Maitree was a postdoctoral researcher at the Washington University School of Medicine in St. Louis. Currently, she is a machine learning R&D engineer at the CCC Information Services Inc., leading cross-functional teams of software engineers and architects on building new generations of enterprise artificial intelligence bots, internet of things applications, and deep learning solutions.

Gloria J. Guzman Perez-Carrillo is the director of the advanced neuroimaging biometrics initiative and assistant residency program director for research at the University of Arizona, Department of Medical Imaging. He has special research interests in advanced neuroimaging techniques, including functional imaging, diffusion spectrum-based imaging, molecular imaging of tumor with F-DOPA in addition to outcomes and translational research of magnetic resonance imaging (MRI) in the field of neuroradiology imaging.

Joshua S. Shimony is a pediatric neuroradiologist working at Saint Louis Children's Hospital and Washington University School of Medicine. His research focuses on developing new techniques and translational applications for MRI methods, resting state functional MRI, diffusion tensor MRI, and perfusion MRI.

H. Michael Gach is a clinical MRI physicist and an associate professor of radiation oncology, radiology, and biomedical engineering at Washington University in St. Louis. His research interests include real-time image acquisition, quantitative hemodynamic MRI (perfusion, diffusion, and flow), MRI-high intensity focused ultrasound and thermometry, MRI-guided radiotherapy, and targeted nanoparticle theranostics. He performs both preclinical and clinical MRI research studies.

Michael Roach is an assistant professor of radiation oncology at Washington University in Saint Louis specializing in stereotactic and adaptive treatments of the thorax and abdomen.

Deshan Yang is an associate professor at the Department of Radiation Oncology, School of Medicine, Washington University in Saint Louis. He is an American Board of Radiology (ABR) certified therapeutic medical physicist. His main research areas include medical image processing and analysis (deformable image registration, image segmentation) for radiation oncology applications, health information technologies, and clinical applications for radiation oncology and medical physics.

Biographies for the other authors are not available.