Regularization Design for High-Quality Cone-Beam CT of Intracranial Hemorrhage using Statistical Reconstruction

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ABSTRACT

Intracranial hemorrhage (ICH) is associated with pathologies such as hemorrhagic stroke and traumatic brain injury. Multi-detector CT is the current front-line imaging modality for detecting ICH (fresh blood contrast 40-80 HU, down to 1 mm). Flat-panel detector (FPD) cone-beam CT (CBCT) offers a potential alternative with a smaller scanner footprint, greater portability, and lower cost potentially well suited to deployment at the point of care outside standard diagnostic radiology and emergency room settings. Previous studies have suggested reliable detection of ICH down to 3 mm in CBCT using high-fidelity artifact correction and penalized weighted least-squared (PWLS) image reconstruction with a post-artifact-correction noise model. However, ICH reconstructed by traditional image regularization exhibits nonuniform spatial resolution and noise due to interaction between the statistical weights and regularization, which potentially degrades the detectability of ICH. In this work, we propose three regularization methods designed to overcome these challenges. The first two compute spatially varying certainty for uniform spatial resolution and noise, respectively. The third computes spatially varying regularization strength to achieve uniform "detectability," combining both spatial resolution and noise in a manner analogous to a delta-function detection task. Experiments were conducted on a CBCT test-bench, and image quality was evaluated for simulated ICH in different regions of an anthropomorphic head. The first two methods improved the uniformity in spatial resolution and noise compared to traditional regularization. The third exhibited the highest uniformity in detectability among all methods and best overall image quality. The proposed regularization provides a valuable means to achieve uniform image quality in CBCT of ICH and is being incorporated in a CBCT prototype for ICH imaging.

Key words: Intracranial hemorrhage, cone-beam CT, model-based iterative reconstruction, spatially varying regularization, detectability, uniform spatial resolution and noise.

1. INTRODUCTION

Intracranial hemorrhage (ICH) is a major cause of death and disability and is associated with a variety of pathologies including hemorrhage stroke, traumatic brain injury, and hypertensive intracerebral hemorrhage.1 Immediate and reliable visualization of ICH is critical to allowing prompt and appropriate medical treatment. Non-contrast-enhanced multi-detector CT is the current front-line imaging modality of ICH, which provides detection of fresh blood in the brain (40-80 HU, down to <1 mm) with high sensitivity but requires transporting the patient to the radiology suite or emergency department.2 As a potential alternative, cone-beam CT (CBCT) offers a small footprint, open adaptable geometry, and relatively low cost, and is potentially suitable for point-of-care deployment in the intensive care unit, urgent care, ambulance, and sports and military theatres. Recent work has demonstrated that scatter and beam hardening artifacts in CBCT can be substantially reduced by high-fidelity artifact correction2, and small ICH lesions can be detected by model-based iterative reconstruction (MBIR) that accurately models variations in noise characteristics following artifact correction4,5.

A challenge associated with ICH detection using CBCT is the spatial nonuniformity in image quality characteristics, including spatial resolution, noise, and the tradeoff between the two. Such nonuniformities are evident in 3D images reconstructed by conventional filtered backprojection or MBIR. For the latter, nonuniform spatial resolution effects
arise primarily from the interaction between the statistical weights and image regularization. Such nonuniformity can be especially significant in CBCT of ICH, because artifact correction (even with appropriately modified statistical weights) significantly alter the magnitude and spatial variation in image noise and correlation. Previous work reported over two orders of magnitude increase in the variations in data fidelity following artifact correction, resulting in visible nonuniformity in spatial resolution and noise characteristics across different regions of the head. Since ICH can occur anywhere in the brain (e.g., subdural hemorrhage close to the cranium versus intraparenchymal hemorrhage deep in the brain parenchyma), such nonuniformity could degrade the detectability of ICH and lead to misdiagnosis.

In this work, we develop image regularization methods to achieve uniform image quality characteristics in CBCT of ICH. Previous work by Fessler et al. proposed a certainty-based method and its variant, showing improved uniformity in either spatial resolution or noise in CT of the chest. In this work, we first leverage the certainty-based method to develop regularization that provides either uniform spatial resolution or noise in a penalized weighted least-squares (PWLS) image reconstruction framework recently developed for CBCT of ICH. The method is then extended to enforce uniform detectability by considering combined properties of contrast, spatial resolution, and noise, and a spatially varying regularization map is designed that encourages uniform detectability for ICH throughout the head. Experiments were conducted on a CBCT test bench using an anthropomorphic head phantom emulating ICH in different regions of the head, and the performance of the proposed regularization methods were compared.

2. METHODS

2.1 Generalized regularization for statistical reconstruction in CBCT

In this work, we adopt a PWLS image reconstruction framework previously developed for CBCT of ICH. The PWLS framework assumes a forward model that involves correction for x-ray scatter and beam hardening before image reconstruction, and the statistical weights are modified based on a model for the change in variance following each correction. The objective function of the PWLS method along with a generalized regularization term can be written as:

$$\hat{\mu} = \arg \min_{\mu} \frac{1}{2} \| A \mu - I \|_W^2 + R(\mu)$$

where $\mu$ is a $N_\mu \times 1$ vector representing the image estimate, $I$ is a $N_\mu \times 1$ vector representing the artifact-corrected line integrals, $A$ is a $N_T \times N_\mu$ matrix denoting the linear projection operator ($A^T$ denoting the linear backprojection operator), and $W$ is a diagonal weighting matrix with the $i$th diagonal element the inverse of the variance of $l_i$ (computed by Eq. (18) in [5]).

The generalized regularization term $R(\mu)$ penalizes first-order neighbor differences by a penalty function $\psi$, which is then weighted by a certainty parameter $\kappa_j$ (described in Sec. 2.2 and 2.3) and a regularization strength parameter $\beta_j$ (described in Sec. 2.4). If the two parameters ($\kappa_j$ and $\beta_j$) are scalar, then the regularization term is controlled simply by a global scalar parameter and is referred to as “traditional” regularization in this work. However, if $\kappa_j$ and $\beta_j$ are allowed to vary spatially, then uniformity in image quality characteristics can be enforced as detailed below.

2.2 Regularization for uniform spatial resolution in ICH

Spatial resolution can be characterized in terms of the local point spread function (PSF), whose approximate analytical form for the PWLS estimator in Eq. (1) can be written as:

$$[\text{PSF}]_j \approx \left[ A^T W A + R \right]^{-1} A^T W A \delta_j$$

where $\delta_j$ is a $N_\mu \times 1$ unit vector with an impulse at the $j$th element, and $R$ is the Hessian of the regularization term $R(\mu)$. Since the statistical weights can undergo large variations between measurements in CT (e.g., strong variations in CBCT of the head as reported in [5]), the Fisher information matrix $A^T W A$ is usually shift-variant, resulting in nonuniform PSF for traditional regularization. We can achieve uniform PSF (or more precisely, uniform peak amplitude of the PSF) by leveraging the certainty-based method proposed by Fessler et al. by computing a spatially varying parameter $\kappa_j^\delta$ (referred to as the “resolution certainty” in this work) in the regularization as:
\[ K_j^R = \left( \frac{\sum_{i=1}^{N_j} a_{ij}^2 W_i}{\sum_{i=1}^{N_j} a_{ij}^2} \right)^{1/2} \] (3)

where \( a_{ij} \) is the \((i,j)\)th element in the matrix \( A \). As seen in Eq. (3), the certainty describes the data fidelity (or weights) of all measurement rays that pass through a given voxel; therefore, certainty is usually high in a high-fidelity region (e.g., near the periphery of the object, where attenuation lengths are lower and transmitted fluence is higher) and low in a low-fidelity region (e.g., near the center of the object and/or in proximity to highly attenuating bone). As a result, the proposed regularization will increase smoothing in high-fidelity regions and reduce smoothing in low-fidelity regions compared to traditional regularization. This is preferable for achieving uniform spatial resolution, since traditional regularization may insufficiently smooth high-fidelity data and over-smooth low-fidelity regions (the latter leading to a strong reduction in spatial resolution in regions of high attenuation). Note that the regularization strength parameter \( \beta_j \) is a scalar in this method as well as the method described in the next section.

2.3 Regularization for uniform noise in ICH

Noise characteristics can be represented by the image covariance matrix, which describes the correlation of noise between one voxel and its neighbors. To achieve uniform noise magnitude, we leverage a variant of the certainty-based method \(^9\) and compute a spatially varying parameter \( K_j^N \) (referred to as the “noise certainty”) in the regularization as (dropping the second term in Eq. (51) in [6] for simplicity):

\[ K_j^N = \left( \frac{\sum_{i=1}^{N_j} a_{ij}^2 W_i}{\sum_{i=1}^{N_j} a_{ij}^2} \right)^{1/4} \] (4)

Similar to the resolution certainty (Sec. 2.2), the noise certainty also tends to increase smoothing in high-fidelity regions and reduce smoothing in low-fidelity regions compared to traditional regularization. However, its spatial dependence is reduced compared to the resolution certainty (evident in the different exponents in Eq. (3) and (4)).

2.4 Regularization for uniform detectability in ICH

It may be desirable to achieve uniform image quality in terms beyond spatial resolution or noise alone - i.e., in terms that combine resolution and noise in a manner relating to detectability. Analogous to the detectability index \(^10\) (a prevalent metric in signal detection theory and image quality optimization), we may consider various forms of ideal observer in weighting the spatial resolution (described by the modulation transfer function, MTF) and noise (described by the noise-power spectrum, NPS) in relation to a given imaging task. Analogous to the nonprewhitening observer model for a delta-function detection task in which all spatial frequencies are equally weighted, we introduce the following figure of merit (FOM) that includes contrast, spatial resolution, and noise in the reconstructed image:

\[ \text{FOM} = c^2 \frac{\int [\text{MTF}(f)]^2 df}{\int \text{NPS}(f) df} \] (5)

where \( c \) denotes the local contrast between the object (ICH) and the background (brain), MTF is the local, contrast-specific modulation transfer function, and NPS is the local noise-power spectrum. While the FOM in Eq. (5) is analogous to the nonprewhitening detectability index (squared) for a delta-function detection task, the FOM can certainly be modified to describe other observer models and/or to describe other imaging tasks that emphasize low or high frequencies.

We propose a two-step approach for achieving uniform FOM. First, the certainty parameter \( K_j \) is computed using Eq. (3) to achieve (nearly) uniform spatial resolution. Second, for each voxel, FOM is computed as a function of the regularization strength parameter \( \beta_j \), and a \( \beta_j \) value can be chosen given a target FOM value. The use of the resolution certainty in the first step simplifies the evaluation of FOM in the second step, since the (local) MTF becomes uniform throughout the image and therefore does not need to be evaluated on a voxel-by-voxel basis.
3. RESULTS AND BREAKTHROUGH WORK

Experiments emulating ICH in an anthropomorphic head phantom were performed on a CBCT test-bench with a flat-panel detector (PaxScan 4343R, Varian, Palo Alto, CA) as shown in Fig. 1(a). A custom head phantom was filled with a gelatin mix and cerebral ventricle models (prepared with wax) to provide contrast equivalent to brain and cerebrospinal fluid, respectively. ICH was simulated by placing plastic spheres (diameter ranging from 1.5 mm to 12 mm) in different regions of the head in the gelatin mixture, resulting in a gelatin-plastic contrast closely simulating that of brain to fresh blood (~50 HU). The phantom was scanned twice at 100 kVp, 144 mAs total (0.4 mAs per projection, 360 projections), and detector binning to $0.556 \times 0.556$ mm$^2$ pixel size. The system geometry presented a $580$ mm source-to-axis distance and $800$ mm source-to-detector distance over a 360° orbit, resembling a potential configuration for compact CBCT system. The two datasets were corrected for scatter and beam hardening and reconstructed with 0.5 mm isotropic voxel size using PWLS with one of the following four regularization methods: (1) traditional regularization ($\kappa_j$ and $\beta_j$), (2) uniform resolution penalty ($\kappa_j^R$ map, scalar $\beta_j$), (3) uniform noise penalty ($\kappa_j^N$ map, scalar $\beta_j$), and (4) uniform detectability penalty ($\kappa_j^D$ map and $\beta_j$ map). A Huber function was used as the penalty function. The ordered-subsets separable quadratic surrogates algorithm$^{11}$ was used to yield a converged PWLS image after 100 iterations (10 subsets).

Image quality was evaluated in three simulated ICH lesions located in various regions of the head. As seen in Fig. 1(b-e), spheres #1 emulates ICH adjacent to the cranium, whereas spheres #2-3 emulate ICH in the deep parenchyma. The spatial resolution at each location was measured by fitting a sigmoid$^{12}$ to the edge spread function (ESF) of each sphere.

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**Figure 1:** (a) Experimental setup on a FPD-CBCT test-bench emulating ICH in an anthropomorphic head phantom. (b-d) Three acrylic spheres selected for image quality evaluation. Sphere #1 emulates ICH adjacent to the cranium, whereas spheres #2-3 emulate ICH in the brain parenchyma. Each pink rectangle denotes a noise ROI for one sphere. The location of each sphere in the $z$ axis is illustrated in (e).

**Figure 2:** Axial (a), sagittal (b), and coronal (c) slices of the resolution certainty $\kappa_j^D$ computed using Eq. (3), showing strong spatial variations over one order of magnitude in the head. The axial slice is in the skull base region (location denoted by the dashed line in the sagittal slice) where the certainty tends to be the lowest (attenuation lengths the highest).
(specifically, fit to all voxels within a 60° fan centered on the sphere and averaged over all the fans) and assessing the width of the sigmoid (referred to as the ESF width). The contrast \( c \) was also estimated from the fit. The noise was calculated as the standard deviation of voxel values in a region of interest (ROI) \((19 \times 19\text{ voxels})\) in a flat region of brain adjacent to a sphere of interest. The contrast- and object-specific local MTF in Eq. (5) was computed by first deriving its analytical expression from the sigmoid and then substituting the sigmoid width estimated from the function fit. The denominator in Eq. (5) is equivalent to variance, which was computed locally throughout the volume as the variance in a neighborhood in a “noise-only” image acquired by subtracting the PWLS images reconstructed from the two scans mentioned above.

Regularization methods were evaluated for uniformity in spatial resolution and noise. Figure 2 shows the resolution certainty \( k^R \) computed in images of the head acquired on the CBCT test-bench according to Eq. (3). Higher certainty can be seen in regions close to the cranium while lower certainty is evident in the parenchyma and skull base, which agrees with the fact that data fidelity tends to be higher in the periphery of the scanned object and lower in the center. The large variations in the data fidelity as estimated by the certainty map (over an order of magnitude) also suggest that the effective smoothing from traditional regularization can vary strongly across the image, leading to nonuniform spatial resolution. Similar spatial variations (but with reduced effect) were found in the noise certainty map (not shown).

Figure 3(a-c) shows the uniformity in spatial resolution for traditional, uniform noise, and uniform resolution penalties. The spatial resolution for the traditional penalty exhibited strong nonuniformity with finer spatial resolution close to the cranium (#1) and coarser resolution in the parenchyma (#2-3). The uniformity in spatial resolution was most improved for the uniform resolution penalty. As shown in Fig. 3(d-e), the noise in traditional penalty was higher in the periphery and lower in the center, and was highly uniform for the uniform noise penalty. Interestingly, the noise was lower in the periphery and higher in the center for the uniform resolution penalty, opposite to the spatial dependence of noise in the traditional penalty.

Images reconstructed using the three regularization methods are shown in Fig. 4 (top three rows). For fair comparison, spatial resolution was matched to that of sphere #3 among three methods by selecting a given \( \beta \) value for each method.

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Figure 3: Comparison of uniformity in spatial resolution (a-c) and noise (d-f) among traditional penalty. As expected, the traditional penalty (a,d) exhibits strong variation in both resolution and noise in various locations (spheres 1-2-3). Also as anticipated, the uniform noise penalty (b,e) exhibits more uniform noise characteristics, and the uniform resolution penalty (c,f) more uniform resolution. For each method, PWLS images were reconstructed using different scalar regularization strength \( \beta \). The error bars are based on the standard derivation of the ESF width or noise in three neighboring axial slices.
Similar to Fig. 3, nonuniform spatial resolution (standard derivation among 3 spheres $\sigma_R = 0.29$ mm) and noise ($\sigma_N = 0.59$ HU) can be seen with the traditional penalty. The nonuniformity for the traditional penalty is most obvious in the skull base, where the data are heavily smoothed due to very low data fidelity. The spatial resolution was more constant for the uniform noise penalty ($\sigma_R = 0.20$ mm) and exhibited the least variation with the uniform resolution penalty ($\sigma_R = 0.04$ mm). The noise was largely constant for the uniform noise penalty ($\sigma_N = 0.17$ HU) but highly variable for the uniform resolution penalty ($\sigma_R = 0.36$ HU). (Note higher noise in the skull base and lower noise close to the cranium).

The performance of the proposed uniform detectability penalty was also evaluated. Figure 5(a) shows FOM as a function of the regularization strength $\beta_j$ for the 3 sphere locations. We note that (almost) any target FOM value can be achieved by selecting proper regularization strength at each location. Figure 5(b) shows one coronal slice of the spatially varying $\beta_j$ map designed for the target FOM value denoted by the dashed line in Fig. 5(a). Spheres reconstructed using this map were shown in Fig. 4 (bottom row). The relative FOM (ratio of FOM to the target FOM, denoted as $FOM_{rel}$) was calculated for all four regularization methods and is also shown in Fig. 4. It can be seen that the FOM was much less variable for the uniform detectability penalty ($\sigma_{FOM_{rel}} = 2.1\%$), compared to the traditional penalty ($\sigma_{FOM_{rel}} = 20\%$), uniform noise penalty ($\sigma_{FOM_{rel}} = 20\%$), and uniform resolution penalty ($\sigma_{FOM_{rel}} = 87\%$). Moreover, one

![Figure 4: Spheres in different regions of the head reconstructed by PWLS with four regularization methods. The spatial resolution was matched to that of sphere #3 for all four methods. Grayscale window: [-10 110] HU.](image)

![Figure 5: (a) FOM as a function of $\beta_j$ at 3 spheres. The dashed line represents the target FOM value selected in this work. (b) One coronal slice of a spatially varying $\beta_j$ map (displayed in log scale and overlaid on a CBCT image) designed to achieve uniform FOM in the image.](image)
finds that the uniform detectability penalty also exhibited the best perceived quality of ICH lesions throughout the head. It may be possible to design an alternative spatially varying $\beta_i$ map to optimize FOM (or other metrics for detectability) everywhere in the image, which is the subject of future work.

4. CONCLUSION AND DISCUSSION

Three image regularization methods were investigated in terms of their ability to yield uniform image quality characteristics in CBCT of the head using a PWLS reconstruction framework. The methods compute regularization according to: 1) spatially varying certainty for uniform spatial resolution; 2) spatially varying certainty for uniform noise; and 3) spatially varying regularization strength for uniform detectability, with a FOM computed in a manner that weighs both spatial resolution (MTF) and noise (NPS) against spatial frequencies of interest in the imaging task. In test-bench experiments emulating ICH in an anthropomorphic head phantom, improved uniformity was achieved for each of the three regularization methods. The proposed task-based FOM regularization provides a potentially valuable means to achieve uniform image quality in CBCT of ICH and allows flexibility in achieving the desired uniformity in spatial resolution, noise, and/or detectability. The proposed regularization methods also motivate further investigation in development of a dedicated point-of-care system for diagnosis of ICH.

The task-based image regularization method proposed in this work presents an interesting concept by which image regularization may be designed not simply based on spatial resolution or noise but in terms of an imaging task and FOM that combines spatial resolution, noise, and spatial frequencies of interest – for example, task-based detectability index. Note also that disparate tasks (and regularization) may be defined in different regions of the image - for example, a low-to-mid frequency task appropriate to low-contrast lesion detection within the brain parenchyma and a distinct high-frequency task appropriate to fracture detection in regions of bone. The use of a task-based metric in regularization design presents a promising approach for “task-based” or "task-driven" regularization design. Preliminary work shown in this paper investigated such task-driven 3D image reconstruction first by considering a simple task-based metric corresponding to an "all-frequency" (delta function) detection task and designed a regularization method that achieved uniform FOM throughout the head, assuming a nonprewhitening observer model. While this work demonstrated feasibility of task-based regularization design, it can be extended in at least two respects. First, one may envision a task that more closely corresponds to ICH detection when computing the task-based metric - for example, a low-contrast, mid-frequency detection task. Second, instead of achieving uniform detectability throughout the head, one may design a regularization method that optimizes (i.e., maximizes) detectability everywhere in the head. This is expected to improve the overall detection of ICH globally compared to the case of enforcing uniform detectability as shown above. The extension of task-based regularization in these two respects is the subject of ongoing work.

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