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End-to-end Modeling for Predicting and Estimating Radiomics: Application to Gray Level Co-occurrence Matrices in CT

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Abstract

While radiomics models are finding increased use in computer-aided diagnostics and as imaging biomarkers for inference and discovery, their utility in computed tomography (CT) is limited by variability of the image properties produced by different CT scanners, imaging protocols, patient anatomy, and an increasingly diverse range of reconstruction and post-processing software. While these effects can be mitigated with careful data curation and standardization of protocols, this is impractical for diverse sources of image data. In this work, we propose to generalize traditional end-to-end imaging system models to include radiomics calculation as an explicit stage. Such a model permits both prediction of the undesirable variability of radiomics, but also forms a basis for inverting the process to estimate the true underlying radiomics. This framework has the potential to provide for standardization of radiomics across imaging conditions permitting more widespread application of radiomics models; larger, more diverse image databases; and improved diagnoses and inferences based on those standardized metrics. We apply this framework to a large class of popular radiomics based on the Gray Level Co-occurrence matrix under conditions of imaging system that are well describe by traditional linear systems approaches as well as nonlinear systems for which traditional analytic models do not apply.

1. INTRODUCTION

Radiomics have been widely used as image biomarkers to aid diagnosis, stage disease, determine treatments, and predict outcomes. With increasing access to large patient image databases, radiomics are also increasingly popular for data mining, inference, and the search for new biomarkers for underlying biological and physiological processes. In research settings, radiomics have shown great potential to obtain more information from imaging studies and to aid the clinical decision making process. A major impediment towards clinical translation is the repeatability and generality of radiomics models.¹ Radiomics are directly computed from the image data and are therefore sensitive to the image properties of those images. For example, the appearance of textures in an image is affected by the intrinsic noise and spatial resolution of that image.² In CT, it is widely known that imaging conditions (x-ray technique, scanner vendor, etc.), reconstruction and post-processing algorithms, and patient anatomy (anatomical site and habitus) imparts variability in noise and resolution.³ This image variability translates to undesirable variability in the radiomics values restricting radiomics models to carefully standardized imaging conditions, making it more difficult to detect weak biomarker signatures, and limiting the ability to aggregate patient image databases from diverse sources. Novel nonlinear processing schemes like model-based iterative reconstruction and machine learning methods pose additional challenges with

different and increasingly scan-dependent image properties that are not well-characterized by simple noise and resolution metrics.

There is an extensive body of work on modeling the image properties of CT. For example, the ability of cascaded model to predict noise and resolution based on imaging parameters and patient anatomical models has been demonstrated and used widely for system design and optimization.³ Consider the first four stages of the cascaded model in Figure 1 where quanta originating at the x-ray source are model through the patient, subject to detection effects, and data processing/reconstruction to predict quantifiable image properties like the modulation transfer function (spatial resolution) and noise (noise power spectrum). In this work, we propose to incorporate radiomics computation as an additional step in the theoretical model such that the variability can be predicted in the same way as image properties. This new end-to-end model treats the imaging system as a measurement device for computation of radiomics. With a predictive model for imaging and radiomics outputs, we also have an opportunity to “invert” the model to recover the underlying ground truth radiomics or standardize them to a common baseline.

In this work, we demonstrate this new paradigm for radiomics calculation wherein the end-to-end model is used to model and remove the undesirable variability associated with the specific imaging conditions. We concentrate on one class of radiomics that are based on the gray level co-occurrence matrix (GLCM). We demonstrate the ability to estimate the underlying radiomics in two scenarios: 1) Where image properties can be considered linear and shift-invariant; and 2) a nonlinear system where image properties are increasing image-dependent and cannot be characterized by traditional analytic expressions.

2. METHODS

We demonstrate the modeling and recovery process for radiomics derived from the GLCM. Specifically, rather than predicting scalar metrics like GLCM-homogeneity, GLCM-correlation, etc. we concentrate on prediction and recovery of the GLCM itself, impacting all derived metrics. Although GLCM computation itself is not linear, we demonstrate in the following section that the effect of noise and resolution on GLCM can be modeled via linear operations.

2.1 Modeling and recovery in linear and shift-invariant systems

Modeling GLCM in the presence of blur and noise: We adopt a general model that can apply to arbitrary imaging systems and conditions. Specifically, we assume that the point spread function of the system (h) and noise (n) of the image are known for the particular imaging conditions and the system is, at least, locally shift-invariant/stationary. Such information can be obtained using empirical measurements of spatial resolution and noise, or derived from well-established system models (e.g., cascaded system analysis). The effect of noise and blur on a GLCM is summarized in (the left half of) Fig.2. To model noisy, blurry data we begin with a ground truth image (x) and apply the known blur. Presuming additive Gaussian noise for all voxels, i.e., $n \sim \mathcal{N}(0, K)$ with covariance K , realizations of that noise may be generated and added to the blurred image to form noisy measurements. However, we note a very important observation: The effect of additive noise

on the GLCM is to blur the GLCM of the blurred image ($G\{h * x\}$) with the GLCM of the noise ($G\{n\}$). Blur and noise each have a significant impact on the GLCM (and subsequent derived scalar radiomics). We have shown GLCM for a 1 pixel offset at 0° below. Note how, in this case, blur narrows the GLCM toward the diagonal, while additive noise tends to spread values. Importantly, both blur and noise prevent accurate estimation of the GLCM directly from measurements.

Recovering the GLCM of the original image: The effect of blur on the GLCM depends on the underlying image (x); however, as observed above we have identified a series of linear operations in modeling the GLCM of the measured data. Thus, one can attempt to recover the original image using linear deblurring operations. This process is noise magnifying – but predictable with the following form: $h^{-1} * y = x + h^{-1} * n$. The deblurring increases noise in the deblurred image and broadens the GLCM. However, as noted above that additive noise may be modeled as the convolution of the original GLCM with the GLCM of that additive noise. Thus, we may model the noise in the deblurred image, form the GLCM, and deblur the GLCM directly to recover the target GLCM as illustrated in the right half of Fig.2.

We perform this recovery on sample simulated data with exactly known blur and noise distributions of the original measurements. To exercise the recovery method as a function of imaging parameters, we simulated the MTF and NPS for an example imaging system at different mAs, and therefore, dose levels. The GLCM was recovered according to the workflow described above. Example derived scalar metrics were computed from the recovered GLCM and compared with ground truth and those computed from the blurry and noisy images.

2.2 Recovery in Nonlinear systems

For imaging systems with nonlinear processing, it is difficult to find an analytic model for radiomics variability. Instead, we propose a data-driven approach for radiomics recovery. The proposed network structure is illustrated in Fig.3 and is inspired by the recovery workflow for linear systems (e.g. deblur, compute GLCM, deblur GLCM), where a first block of convolutional neural network (CNN) acting on the blurry noisy image input is followed by an untrainable radiomics computation layer, followed by another block of CNN acting directly in the radiomics domain. The CNN architecture is based on the residual encoder architecture (REDNet⁴) with two skip connections.

To increase diversity of the training data and improve generality of the network, we performed training using high resolution photographs from the DIV2K dataset.⁵ The high resolution images were treated as ground truth, normalized to a range comparable with linear attenuation coefficients (0 0.05), forward projected, and reconstructed using a nonlinear (and non locally linearizable) reconstruction algorithm - penalized-likelihood reconstruction with a Huber penalty (PLH). The reconstructed images and the GLCM of the ground truth image form the input and output of the network. We used a total of 650 64×64 image patches for training and 150 distinct patches for testing. The network was optimized using the Adam optimizer over 2000 epochs.

3. RESULTS

Quantitative results for recovery in the linear system example are shown in Fig.4 and 5. Four example derived scalar radiomics values from the GLCM - contrast, correlation, energy, and homogeneity, are shown as a function of mAs (Fig.4) and cutoff frequency (Fig.5). The ground truth is independent of exposure and is plotted as a straight line. All metrics from the blurred and noisy images deviate from ground truth, while metrics computed from the recovered GLCM show close agreement with the ground truth at most mAs levels. At the lowest mAs, noise amplification from the first deconvolution step becomes too severe for the recovery to work well.

Recovery results for the nonlinear imaging system with PLH reconstruction is shown in Fig.6. From the 150 testing cases, we show the best, mean, and worse performance in terms of the loss function. The network exhibits good capability to recover GLCM of various structures for the best and mean performance cases. In the worst performance case, we were unable to recover the truth GLCM. This image contains high frequency details that likely dominate the ground truth GLCM structure. Blur and noise imparted by the projection and reconstruction likely created a null-space that prevents specific information from being recovered. Thus, for standardization, the true underlying radiomics (at the finest resolution) may not be an achievable goal across all scanning conditions. Instead, it would be more appropriate to find a lower resolution surrogate to serve as “truth”.

4. CONCLUSIONS

We proposed an end-to-end modeling approach for predicting and recovering radiomics. The end-to-end model explicitly includes radiomics computation as an additional step to existing theoretical models of the imaging chain, thereby relating various acquisition and reconstruction parameters to radiomics variability. We developed methods to recover ground truth radiomics values based on known noise and resolution in a linear system, and demonstrated recovered radiomics values in close agreement with the ground truth. For nonlinear systems where the noise and resolution cannot be easily characterized, we proposed a data-driven approach using network architecture informed by the recovery workflow in linear systems. The network demonstrated good ability to recover the GLCM up to a point. For images with GLCMs that represent very high frequency structures/textures, it is not always possible to perform the inversion (information is lost/part of a system null space that is not recoverable). In this case, a lower resolution baseline protocol can be adopted. In ongoing work, we will further investigate such limits and baseline protocols, develop the framework to encompass a wider range of data processing algorithms, and evaluate the accuracy of the recovered radiomics in physical experiments.

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Figure 1:

We propose to model radiomics computation as an additional step in existing models of the imaging systems, thereby relating intrinsic noise and resolution in the image data to radiomics variability.

Figure 2:
Prediction and recovery of GLCM in a linear and shift-invariant system.

Figure 3:

Network structure for radiomics recovery in general nonlinear systems. The structure echoes the linear recovery workflow with a CNN block acting in the image domain, a connecting, untrainable layer that computes radiomics, and another CNN block acting in the radiomics domain.

Figure 4:
Example radiomics features computed from the GLCM matrices as a function of mAs.

Figure 5:
Example radiomics features computed from the GLCM matrices as a function of mAs.

Figure 6: Radiomics recovery in a nonlinear imaging system with penalized likelihood reconstruction with a Huber penalty. The best, mean, and worse performance cases out of the 150 test cases are shown.