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研究課題名（和文）Development of an acoustic imaging modality for absolute and real-time radiotherapy dosimetry

研究課題名（英文）Development of an acoustic imaging modality for absolute and real-time radiotherapy dosimetry

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研究成果の概要（和文）：放射線治療における線量分布とそれに伴う音波を計算する手法を考案し、X線照射条件の変化による音波への影響を検討した。一般的なX線照射法では照射時間が長く効果的に音波を計測できない。音波再構成画像の画質は音波発生源から受信機までの距離、受信機の数や配置などに影響する。受信機を大量に設置するとX線照射野を塞いでしまう問題がある。
音波画像と線量分布を定量的に計算するため、患者の解剖学的構造をリアルタイムで追跡できる高度画像再構成法を開発した。放射線治療装置に付属できる三次元体表面計測装置を用いて患者の動きを計測し、CT画像を現在の体構造に合わせた。本手法は従来法に比べ高速に解剖学的構造を追跡できた。

研究成果の学術的意義や社会的意義
X-ray-induced acoustics could be realized for absolute dosimetry in radiotherapy, if clinical systems are setup with shorter beam lengths and sensor array designs are balanced between anatomy coverage and beam obstruction. To do so in real-time could be facilitated by neural image reconstruction.

研究成果の概要（英文）：A framework for simulation of radiotherapy dose deposition and induced acoustic wave production was developed. X-ray beam parameter dependency of induced acoustics was reviewed. Standard clinical radiotherapy system setups are not ideal given beam length is long. Significant reconstruction artifacts exist proportional to distance from transducer elements as well to completeness in coverage by distribution of sensor arrays, though physically obstructing the irradiating beam's path also an issue.
Knowledge of exact tissue properties is critical for quantitative acoustic imaging and accurate dosimetry, especially in real-time as the body moves during treatment. Efforts were focused on investigation of advanced image reconstruction and artifact reduction methods. On-board and body surface depth imaging were used as motion surrogates to render higher quality planning CT. Performance competitive, if not superior, to state-of-the-art techniques were apparent in accuracy and inference speed.

研究分野：物理学、医学、工学

キーワード：CT reconstruction　Machine learning　Radiotherapy　Dosimetry　Acoustic imaging

１．研究開始当初の背景

X-ray-induced acoustic (XA) imaging, an extension of photoacoustic imaging, is a novel modality capable of producing an image of the differential pressure distribution in a medium after irradiation by an ionizing photon[1–3]. Both methods rely on the photoacoustic (PA) effect describing conversion between light and acoustic waves, though XA is far less subject to the well-known drawback of depth limitation seen by traditional PA due to limited penetration of optical and/or infrared photons.

In both XA and PA, deposition of heat energy from absorption of a photon beam within a material leads to localized temperature increase, causing thermoelastic expansion, induction of a differential pressure distribution, and generation of acoustic waves propagating through the medium. The properties of these acoustic waves are inherently dependent on the amount of heat energy deposited, the shape of the energy distribution of a radiation pulse, and the material properties of the medium. Any fractional change in tissue characteristic translates into an equal amount of fractional change in the XA signal.

As contrast in X-ray-induced computed tomography (XACT) is dependent upon a material's differing X-ray absorption properties, the technique has long been proposed and more recently shown as having potential applications for dosimetry in radiotherapy[4]. It has been shown that onsite radiation dose information can be derived by XA amplitude and in this way, XACT can help improve precision of radiation therapy and optimize treatment strategy[5,6].

There are several benefits of dosimetry using XACT. XACT does not disturb the photon beam, eliminating correction factors required by many other dosimetry techniques. Additionally, induced XA signals are linearly related to the amount of dose deposited and are energy independent over photon energies. Using related pressure to deposited dose, XACT could be used as an absolute dosimetry technique provided tissue properties are accurately determined and transducer is well defined and calibrated[7,8]. In a clinical setting, such tissue properties (tissue density and Grüneisen coefficient) may be derived from a CT scan, though they are not typically performed prior to every treatment fraction. However, it may be possible to deform the planning CT scan based on the radiotherapy system's on-board imaging or other body motion surrogate to adapt XACT for absolute real-time dosimetry by exploiting advanced image processing techniques able to solve such inverse problems. Dimension reduction[9], machine learning[10], and compressed sensing[11] methods can be utilized for reconstruction of clinical images generated from undersampled data, at greatly accelerated speeds, if not in real-time. Combining these techniques with XACT would allow for improvements toward the development of adaptive radiation therapy (ART).

In typical fractionated treatment schemes, patients receive radiation over the course of many weeks, during which patient anatomy changes due to factors such as tumor shrinkage and weight loss. Therefore, the planning CT and the developed treatment plan may no longer accurately represent the patient's anatomy. ART is a process by which a patient's treatment plan is modified over the course of therapy to reflect such changes. This can be done by performing additional planning CT images and creating new plans during the treatment period, though re-planning based on daily imaging prior to treatment is a demanding process requiring advanced software techniques for rapid image reconstruction, contouring, and dose simulation. Truly realizing ART would mean incorporating such advanced techniques into a real-time process.

２．研究の目的

Acoustic signals produced by tissues irradiated by X-rays during radiotherapy have potential to be exploited for dosimetry. The method has the potential to measure absolute dose absorbed in vivo in real-time. Hence, our study focused on two specific aims: 1) Develop a comprehensive framework to characterize the performance of an XACT dosimetry for radiation therapy; 2) Develop advanced image reconstruction methods for use with XACT and other aspects of ART.

３．研究の方法

Development of a novel imaging strategy for absolute and real-time in vivo dosimetry in radiotherapy represents an important step in the increase in demand and necessity for an accurate method of ART. Such a modality stimulates production of acoustic signals from X-ray absorbing tissues, which are simultaneously collected using an ultrasound detector array to provide complimentary 3D information of delivered dose distribution. This study investigated the principle and implementation of an XACT system for absolute dosimetry.

A comprehensive framework relying on a simulation workflow and experimental measurements to systematically evaluate the properties of LINAC irradiation-induced acoustics and calibrate the XACT system was developed, allowing for comprehensive modeling of both stages of XACT dosimetry: dose deposition and acoustic wave signal production. The resulting platform was applied to several irradiation situations simulated with Monte Carlo. Signal dependency on a number of factors, including radiation dose, beam energy, pulse width, object size, object position, transducer sensitivity, and noise sources was examined to allow prediction of spatial resolution and image quality.

We investigated the use of several advanced image reconstruction techniques, such as machine learning and compressed sensing methods in the rendering of high-quality CT images generated from the therapy planning CT image and guided by undersampled representations obtained by on-board imaging device, as well as body surface depth imaging, during treatment. How effective the methods were able to remove scatter, reduce artifacts, and reconstruct 3D images allowing for exacting tissue properties were reviewed. Some surrogate is necessary in calculating absolute dose absorbed by irradiated tissue in real-time using XACT, in order to mitigate the problem of full CT images not being obtained before each treatment fraction.

While this study focused on the development of a dosimetry system for radiotherapy and translation into the clinic for this purpose, the concept and strategy is extendable to other clinical applications as well, such as particle beam therapy. Advanced techniques were also briefly reviewed for image reconstruction and dosimetry with this modality.

４．研究成果

System design for collecting acoustic signals induced by irradiation was completed and hardware procured. A local research LINAC radiotherapy system was characterized and considerations taken for use in this study.

A framework for numerical simulation of both stages of radiotherapy and induced acoustics for the purposes of dosimetry was developed, making use of the 4D human XCAT phantom and GATE/Geant4 Monte Carlo photon/physics simulator for modeling dose deposition, as well as the k-Wave acoustics wave simulator and MATLAB for modeling acoustic wave signal production. 3D acoustic wave simulations were performed of hardware procured. Significant artifacts were found in experiments proportional to distance from transducer elements as well to completeness in coverage of anatomy by distribution of sensor arrays. Attempts were made modeling US transducer designs as arcs and partial spheres more optimal for 3D imaging, but further exploration is necessary to find balance in a tradeoff between accuracy and sensors being physical obstructions themselves for the irradiating beam's path.

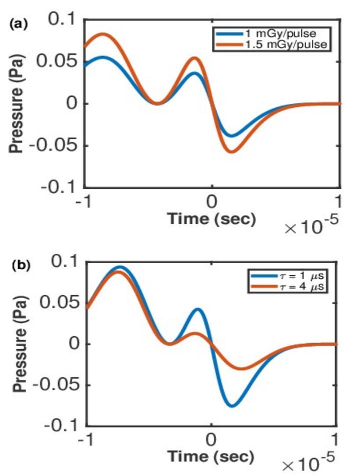

Figure 1. (a) Acoustic signals induced by X-ray pulses delivering 1 or 1.5 mGy dose per pulse with fixed pulse duration absorption cross section and (b) by pulses 1 μs or 4 μs in length.

X-ray beam parameter dependency of induced acoustic signals was reviewed analytically[12]. Induced acoustic signals should be observable in conventional cancer radiotherapy. In contrast with how XACT may perform as a method for parallel imaging on diagnostic X-ray modalities[13], XA signals from the significantly higher energy beams of radiotherapy systems should see modest gains (Fig. 1a). However, longer irradiation beam lengths (pulse duration >1μs) were shown to greatly attenuate magnitude of induced waves (Fig. 1b), which would complicate tomographic reconstruction. Hence, standard clinical radiotherapy system setups may not be ideal with beam pulse lengths usually on order of several ms. Our proposed analytic model is a very simple and practical way of predicting and interpreting these signals in the therapeutic range of beam parameters. The model has a tissue-dependent absorption cross section which is assumed to be based only on the field size here, but this can be further generalized provided that further experimental studies are conducted.

Focus then shifted to 3D image reconstruction for estimation of exact tissue properties real-time during therapy, a necessary component in parallel absolute dosimetric imaging. Several advanced image processing techniques were investigated for metal artifact reduction; sparse and neural reconstruction.

Metal implants are known to cause artifacts in CT images, which adversely affect accuracy in tissue characterization and radiotherapy. Metal artifact reduction (MAR) methods usually approach the problem by restoring projection data corrupted by metals via use of handcrafted priors, such as linear interpolation (LI) or normalization (NMAR). We proposed an MAR method to restore CT sinograms with a data-driven deep image prior (DIP) and found that by using the proposed sinogram handling strategy and generative DIP-based inpainting technique, the projection data through metals can be restored very well, leading to drastically improved image reconstruction[14]. For example, standard deviation of the waterequivalent region in a CT phantom is lowest (0.0105/cm) for our proposed DIP as can be seen in Fig. 2.

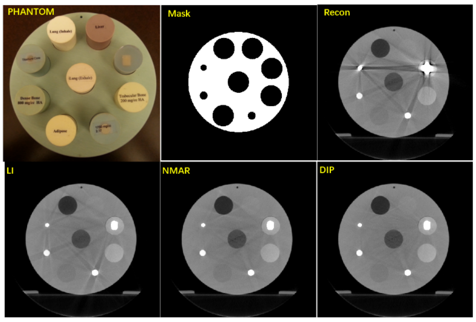

Figure 2. The results from real measurements of CIRS phantom. The 1st row shows the phantom, mask for quantitative evaluation and reconstruction without MAR. The 2nd row shows MAR reconstructions by LI, NMAR, and the proposed DIP method.

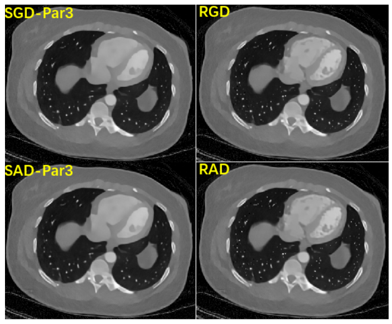

Figure 3. Reconstruction results of real data. SGD indicates conventional single dictionary-based reconstructions using optimal parameterization for a specific tissue region. RGD and RAD indicates the improvements of the proposed region-specific dictionary learning-based reconstructions.

We also present a dictionary learning-based method with region-specific image patches to maximize the utility of the powerful sparse data processing technique for CT image reconstruction[15]. Considering heterogeneous distributions of image features and noise in CT, region-specific customization of dictionaries is useful in iterative reconstruction. Thoracic CT images are partitioned into several regions according to their structural and noise characteristics. Dictionaries specific to each region are then learned from the segmented thoracic CT images and applied to subsequent image reconstruction of the region. Parameters for dictionary learning and sparse representation are determined according to the structural and noise properties of each region. The proposed method results in better performance than the conventional reconstruction based on a single dictionary in recovering structures and suppressing noise in both simulation and human CT imaging (Fig. 3). Quantitatively, the simulation study shows maximum improvement of image quality for the whole thorax can achieve 4.88% and 11.1% in terms of the Structural Similarity (SSIM) and Root Mean Square Error (RMSE) indices, respectively. The proposed strategy takes into account inherent regional differences inside of the reconstructed object and leads to improved images. The method can be readily extended to CT imaging of other anatomical regions and other applications as well.

Current state-of-the-art techniques for solving such inverse problems as CT reconstruction often use flavors of deep neural networks. We investigated the effectiveness of the these advanced machine learning methods for deforming patient CT scans acquired during the planning stage of therapy[16]. In order to adapt this CT for use during actual therapy irradiation in real-time, on-board X-ray and body surface depth imaging were used as motion surrogates to inform reconstruction of the higher quality pre-therapy planning CT. A 2D to 3D deep residual neural network (ResNet, Fig. 4) was trained on synthetic torso images (2D X-ray projections from CBCT imagers or body surface maps from overhead depth camera and corresponding 3D CT) produced using the 4D XCAT Phantom, a highly detailed computerized phantom modeled to provide accurate human anatomy and physiology using CT from a normal subject, including cardiac and respiratory motion. Quantitative performance metrics comparing new CT generated from unseen 2D surface maps against ground truth were reviewed. Comparison with use of on-board X-ray imaging surrogates was also conducted. With single unseen body surface depth maps, new CT could be generated near-real-time at high accuracy with our proposed model (Mean Absolute Error=0.0241, SSIM=0.9383, Peak Signal to Noise Ratio=22.2984).

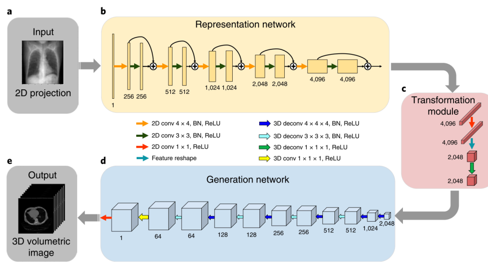

Figure 4. Architecture of the 2D to 3D ResNet. Input of the model are projection views of on-board X-ray and/or depth imagers, output are corresponding volumetric CT.

Lastly, we also investigated performance of the latest architecture deep neural nets in related tasks, involving CT applications in particle beam irradiation, which are also known to induce acoustic signals proportional to dose deposited. We show ResNets are effectively able to reconstruct dose from CT and treatment plan parameters near-instantaneously[17], a valuable tool that could be used in concert with acoustic imaging for dose verification. Furthermore, in a proposal of an image correction method with uncertainty quantification using a Bayesian convolutional neural network (CNN), we show CNN-corrected images represented noise-free images with high accuracy[18]. The aleatoric and epistemic uncertainties that could be calculated simultaneously with such methods were well correlated with an absolute difference between output and label (Fig. 5). The ability to correct CT of noise and quantify inherent uncertainty will not only be tremendously valuable in several aspects of realizing image reconstruction in acoustic dosimetry, but also to image-guided therapy in general.

Knowledge of exact tissue properties is critical for quantitative acoustic imaging as a method of dosimetry, especially as the tissues deform during 4D treatment due to breathing and movement. Hence, to develop a method of reconstructing high quality CT images accurately became the main focus for the project. Deep neural networks prove extremely effective and most impressive at generating novel views of CT in 3D built from robust priors learned, even if only informed with single 2D surrogates. Use of neural reconstruction and inclusion of body surface imagers in addition to established X-ray motion surrogates, such as CBCT, could be very useful in image-guided interventional procedures like ART. Several applications of these techniques to correct image noise and artifacts were also investigated. Performance competitive, if not superior, to state-of-the-art techniques were apparent in accuracy and inference speed. In the latter, reconstruction calculations took only fractions of a second. A significant advance toward realizing use for absolute metrics in real-time.

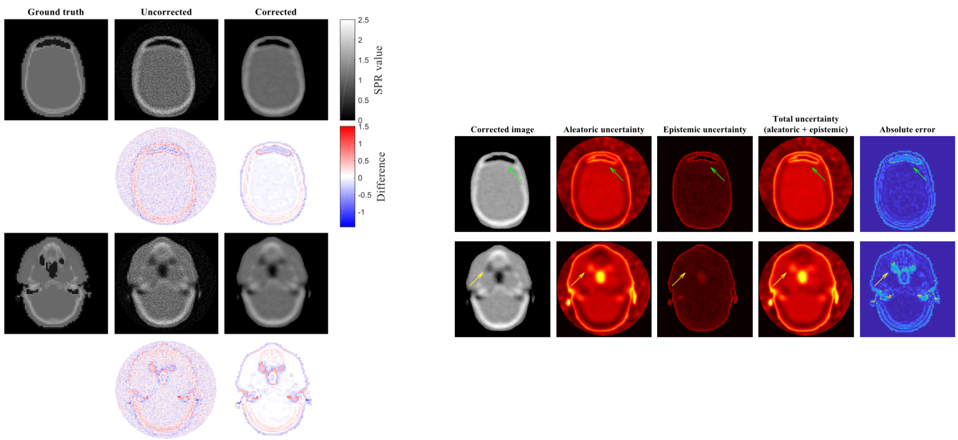

Figure 5. Comparison of the uncorrected and corrected images with the ground truth in two different slices (left). As well, comparison of the aleatoric and epistemic uncertainties with an absolute error of corrected image in same slices (right). Both uncertainties correlate some regions of the absolute errors shown by a green arrow. On the other hand, only one uncertainty well correlates the absolute error at a region shown by a yellow arrow, which helps to identify the potential cause of error.

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５．主な発表論文等

〔雑誌論文〕　計3件（うち査読付論文　3件／うち国際共著　3件／うちオープンアクセス　0件）

１．著者名 Jeff Wang, Qiong Xu, Hiroki Shirato, Lei Xing	４．巻 TBA
２．論文標題 Region-specific Dictionary Learning-based Low-dose Thoracic CT Reconstruction	５．発行年 2020年
３．雑誌名 Transactions on Medical Imaging	６．最初と最後の頁 TBA
掲載論文のDOI（デジタルオブジェクト識別子） TBA	査読の有無 有
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 該当する

１．著者名 Yusuke Nomura, Jeff Wang, Hiroki Shirato, Shinichi Shimizu, Lei Xing	４．巻 TBA
２．論文標題 Fast spot-scanning proton dose calculation method using a three-dimensional convolutional neural network	５．発行年 2020年
３．雑誌名 Physics in Medicine and Biology	６．最初と最後の頁 TBA
掲載論文のDOI（デジタルオブジェクト識別子） TBA	査読の有無 有
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１．著者名 Jeff Wang, Yusuke Nomura, Naoki Miyamoto, Lei Xing, Hiroki Shirato	４．巻 TBA
２．論文標題 Neural reconstruction of volumetric computed tomography from a body surface depth motion surrogate	５．発行年 2020年
３．雑誌名 Physics in Medicine and Biology	６．最初と最後の頁 TBA
掲載論文のDOI（デジタルオブジェクト識別子） TBA	査読の有無 有
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〔学会発表〕　計6件（うち招待講演　3件／うち国際学会　6件）

１．発表者名 Jeff Wang, Qiong Xu, Hiroki Shirato, Lei Xing
２．発表標題 Metal Artifact Reduction with a Deep Image Prior
３．学会等名 American Association of Physicists in Medicine (AAPM) Annual Meeting（招待講演）（国際学会）
４．発表年 2018年

1．発表者名 Canberk Sanli, Jeff Wang, Mehmet Burcin Unlu
2．発表標題 Absorption Dependence of the X-Ray Induced Acoustic Waves
3．学会等名 American Association of Physicists in Medicine (AAPM) Annual Meeting（国際学会）
4．発表年 2018年

1．発表者名 Jeff Wang, Yusuke Nomura, Hiroki Shirato, Lei Xing, Hao Peng
2．発表標題 Feasibility of X-Ray-Induced Acoustic Computed Tomography for Breast Imaging by Monte Carlo Simulation
3．学会等名 American Association of Physicists in Medicine (AAPM) Annual Meeting（国際学会）
4．発表年 2019年

1．発表者名 Yusuke Nomura, Jeff Wang, Hiroki Shirato, Shinichi Shimizu, Lei Xing
2．発表標題 Fast Spot-Scanning Proton Dose Calculation Method with a 3-Dimensional Convolutional Neural Network
3．学会等名 American Association of Physicists in Medicine (AAPM) Annual Meeting（招待講演）（国際学会）
4．発表年 2019年

1．発表者名 Yusuke Nomura, Sodai Tanaka, Jeff Wang, Hiroki Shirato, Shinichi Shimizu, Lei Xing
2．発表標題 Uncertainty-aware reconstructed image correction for proton computed tomography using Bayesian deep learning
3．学会等名 American Association of Physicists in Medicine (AAPM) Annual Meeting（招待講演）（国際学会）
4．発表年 2020年

１．発表者名 Jeff Wang, Yusuke Nomura, Naoki Miyamoto, Lei Xing, Hiroki Shirato
２．発表標題 Neural reconstruction of volumetric computed tomography from a body surface depth motion surrogate
３．学会等名 Annual meeting of the Japanese Society for Radiation Oncology（国際学会）
４．発表年 2020年

〔図書〕　計0件

〔産業財産権〕

〔その他〕

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６．研究組織

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