京都大学	博士（人間健康科学）	氏　名	周　徳軍
論文題目	Development of a deep learning-based patient-specific target contour prediction model for markerless tumor positioning (マーカーレス腫瘍位置決めを目的とした深層学習に基づく患者固有標的輪郭予測モデルの開発)		

（論文内容の要旨）

The tumors located in the lung, liver, and pancreas move with respiration. The real-time tumor tracking (RTTT) method can track the positions of moving tumors at short intervals and guide the treatment beam directly to the tumor, thereby greatly reducing the dose to healthy organs.

Currently, in clinical practice, the kV X-ray imaging technique together with internal markers implanted into the patient's body is the most widely used approach to track the motion of tumors. To realize RTTT, metallic markers are first implanted into the tumor or its surrounding tissue before a computed tomography (CT) scan. Second, the geometric correlation between the internal markers and the tumor is determined in CT. Finally, the position of the tumor can be determined using the geometric correlation by detecting the internal makers on X-ray projection images.

After years of clinical practice, the limitations of marker-implanted RTTT are becoming clear. The implementation of internal markers is invasive and causes potential risks to the patients. From the day of the CT scan until the day of the last treatment, markers may migrate inside the patient's body. Also, markers may not move perfectly simultaneously with the tumor during treatment. These marker-induced tracking errors decrease the accuracy of tumor tracking.

This doctoral dissertation is aiming at developing a deep learning-based patient-specific target contour prediction model for markerless RTTT. Deep learning-based markerless RTTT may overcome the above limitations by directly predicting the position of the tumor in kV X-ray projection images without the assistance of markers. The following is the summary of the dissertation.

A total of fourteen patients with pancreatic cancer were included. All patients underwent the four-dimensional CT (4DCT) scan. The 4DCT images with respiratory signal data were reconstructed and sorted into 10 respiratory phases. Thereafter, oncologists draw the target for each phase.

The data augmentation procedure was conducted to generate enough data to train and test the deep learning model. To augment the data scale, first, we tilted the CT volumes around the superior-inferior and anterior-posterior directions from −3° to 3° in 1.5° intervals. Original digitally reconstructed radiograph (DRR) images and target-only DRR images were then generated from the CT volumes for each patient and each kV X-ray source angle. Subsequently, the Super-SloMo model was adapted to interpolate DRR images between consecutive respiratory phases. In total, the data augmentation procedure yielded the data scale 250-fold. A dataset of 2500 DRR images labeled with target contour was acquired for each patient and each kV X-ray source angle. We randomly split the dataset into a training dataset, which contained 2000 DRR images, and a testing dataset, which contained 500 DRR images.

A specific target contour prediction model was trained and tested with the corresponding DRR image dataset for each patient and each kV X-ray tube angle. To evaluate the performance of the model, two criteria were introduced. The dice similarity coefficient (DSC) was introduced to evaluate the performance of the target contour prediction. The three-dimensional (3D) position of the target was calculated based on the orthogonal centroids of the contour. The 3D error between the ground truth and predicted position was calculated to evaluate the tracking accuracy.

During testing, the mean contour prediction time per image was 55 ms. This fulfills the requirement of RTTT. The model can predict target contour dynamically. Even when the target was overlapping with the bone structure, the model can give accurate contour prediction results. The mean and standard deviation (SD) of the DSC were 0.98 and 0.015, respectively. The mean and SD of the 3D error were 0.29 mm and 0.14 mm, respectively.

The dissertation provides a potential solution for markerless RTTT. In the future, once the clinical feasibility of the model is confirmed and the model is applied in clinical practice, this research will contribute to both the hospitals and patients. For the hospitals, there is no need to change the radiotherapy machine currently for marker-implanted RTTT. The machine can be upgraded to markerless RTTT by just upgrading the software. Also, marker implantation surgery will not be needed anymore. The patients will be freed from potential risks caused by the invasive marker implantation procedure. Marker-induced tracking errors will also be eliminated. The treatment beam irradiation accuracy will be improved, and the healthy organs will be better protected. Our proposed technique will benefit more patients in need and improve the efficacy of RTTT radiotherapy.

（論文審査の結果の要旨）

動体追尾照射とは，標的の呼吸性移動に応じて照射位置を自動的に調整し，標的に限局して放射線を投与することができる照射法である．本照射法を臨床適用する場合，標的近傍に金属マーカーを留置することが一般的であるが，留置に伴う侵襲や金属マーカー位置変位が臨床上の問題となっている．そこで本研究では，金属マーカーを留置せずに直交デジタル再構成 X 線画像(Digitally Reconstructed Radiograph：DRR)上で標的輪郭を予測できる深層学習モデルを開発した．

直交kV-X線撮像システムを有する放射線治療装置を用いて6方向から動体追尾照射を実施した膵癌患者 14 例を対象としたまず，10 呼吸位相に分割された標的輪郭付き 4 次元 CT を頭尾・背腹方向にそれぞれ 1.5°間隔で-30 から 30 回転させ，kV -X 線撮影角度毎に 250 対の DRR と標的のみが抽出された DRR を生成した．次に，両 DRR に対して Super-SloMo モデルを適用し，データ数を 10 倍に拡張した．2500 対のデータのうち，2000 対から深層学習モデルを構築し，

残り 500 対で評価した．この工程を全 12 方向の kV-X 線撮影角度に対して実施した．ダイス係数および 3 次元位置誤差の平均土標準偏差はそれぞれ 0. 98 士 0. 015 および 0. 29 士 0.14mm であった．標的輪郭予測に要する時間は 1 枚の DRR につき平均で 55 ミリ秒であった

本検討は深層学習に基づく標的輪郭予測の精度および時間は臨床的に許容内であることを明らかにしたものである．以上の研究により，動体追尾照射の非侵襲化ならびに高精度化に寄与できることが期待される．

したがって，本論文は博士（人間健康科学）の学位論文として価値あるものと認める．なお，本学位授与申請者は，令和 5 年 1 月 4 日実施の論文審査とそれに関連した試問を受け，合格と認められたものである．

要旨公開可能日：　　　　年　　月　　日　以降