### ARTICLE IN PRESS

Radiotherapy and Oncology xxx (2018) xxx-xxx



Contents lists available at ScienceDirect

# Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



#### Original article

## Retrospective self-sorted 4D-MRI for the liver

Tessa N. van de Lindt\*, Martin F. Fast, Uulke A. van der Heide, Jan-Jakob Sonke

Department of Radiation Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands

#### ARTICLE INFO

Article history: Received 23 June 2017 Received in revised form 4 May 2018 Accepted 4 May 2018 Available online xxxx

Keywords: Respiratory motion 4D-MRI MRI-guidance Liver MR-Linac Self-gating

#### ABSTRACT

Purpose: Daily MRI-guidance for liver radiotherapy is becoming possible on an MR-Linac. The purpose of this study was to develop a 4D-MRI strategy using an image-based respiratory signal with an acquisitionreconstruction time <5 min, providing T2-weighting for non-contrast enhanced tumor visibility.

Materials and Methods: Images were acquired using an axial multi-slice 2D Turbo Spin Echo (TSE) sequence, repeated a variable number of times (dynamics). A self-sorting signal (SsS) was retrieved from the data by computing correlation coefficients between all acquired slices. Images were sorted into 10 phases and missing data were interpolated. The method was validated in a phantom and 10 healthy volunteers. The SsS, image quality (SSIM index: structural similarity index) and quantified liver motion were assessed as a function of the number of dynamics. Tumor visibility was demonstrated in two patients with liver metastasis on the Elekta Unity MR-Linac.

Results: SsS was in good agreement with the reference navigator signal. Missing data increased from  $0.4 \pm 0.6\%$  to  $37.1 \pm 6.6\%$  for 60 to 10 dynamics. The SSIM index for the interpolated slices was  $\sim 0.6$ . The RMSD of quantified motion was <1 mm in phantom experiments and in volunteers <1 mm for >10 dynamics.

Conclusion: For 30 dynamics, acquisition-reconstruction time was <5 min and showed good performance in the validation experiments. The tumor was clearly visible in the patient images.

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Soft-tissue contrast of cone-beam CT (CBCT) is poor in upperabdominal sites, such as the liver, and limits the accuracy of image-guided RT. The clinical introduction of an MRI-scanner integrated with a linear accelerator (MR-Linac) provides superior soft tissue contrast in the treatment room and thus has the potential to increase the accuracy of RT delivery in the upper abdomen. For patients treated free-breathing, 4D-MRI methods for daily patient set-up and motion quantification are required for disease sites subject to respiratory motion. Essential for so-called pre-beam 4D-MRI, is a fast acquisition and reconstruction time (<5 min) to minimize changes between imaging and treatment and to reduce the prolonged MR-Linac treatment fraction timeslots due to pre-beam re-planning and longer treatment delivery times. Another important requirement for daily imaging is good tumor visibility without the use of a contrast agent or implanted fiducials. This has been shown to be achievable with T2-weighted imaging for liver lesions [1-5].

Over the past ten years, several 4D-MRI techniques haven been reported. Most 4D-MRI methods based on the acquisition of 2D slices [6-10] have acquisition-reconstruction times in the order

E-mail address: j.sonke@nki.nl (T.N. van de Lindt).

of minutes and use image sorting according to different respiratory surrogates. However, respiratory motion derived from external surrogates, such as a pressure belt, can deviate from internal motion [11,12] and mounting an external surrogate device is inconvenient for patient-setup. The use of an internal navigatorchannel [6] prolongs acquisition time and can disturb the image acquisition and vice versa, especially when the images are acquired axially. In self-gating methods, the respiratory signal is derived from the acquired data. However, in such a method recently reported by Paganelli et al. [10], images are acquired sagittally and therefore a substantial number of slices is required to provide sufficient FOV-coverage in left-right (LR) direction at the cost of acquisition time [12].

Lately, there has been great interest in self-gated 4D-MRI methods based on 3D sequences [13-16]. Since they provide higher SNR compared to 2D sequences, they have the potential to obtain better spatial resolution. With high k-space under-sampling fast acquisition times ( $\sim$ 1 min) can be achieved [15]. However, this can lead to extensive reconstruction times [16] or the need for a dedicated reconstruction server [15] as reported in literature. Also, these methods do not provide T2-weighted contrast and require vendor-specific or non-commercial pulse-sequences and reconstruction methods and are therefore not widely available at the moment

https://doi.org/10.1016/j.radonc.2018.05.006 0167-8140/© 2018 Elsevier B.V. All rights reserved.

<sup>\*</sup> Corresponding author at: Department of Radiation Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands,

2 4D-MRI for the liver

A 4D-MRI method to overcome the above mentioned challenges was developed and evaluated for daily pre-beam liver imaging on the MR-Linac. The method is based on an axial acquisition to optimize FOV-coverage of the liver, organs at risk and the full body contour with respect to acquisition time. Also, because the dominant liver motion is in CC-direction, axial acquisition leads to minimal in-plane liver motion. Axial images are most familiar to radiation oncologists and easy to integrate with clinical software packages such as the MR-Linac treatment planning system. A novel method to extract a respiratory signal from the axial data was developed to eliminate the need for an additional respiratory surrogate. The method provides a T2-weighted contrast and the respiratory signal is extracted from the images. It uses a standard TSE pulse-sequence and straight forward image reconstruction for easy implementation into the clinic. The quality of the extracted respiratory signal, image quality of the 4D-MRI reconstructions and accuracy of the time-resolved motion were assessed with respect to acquisition time.

#### **Materials & methods**

#### Retrospective self-sorted 4D-MRI

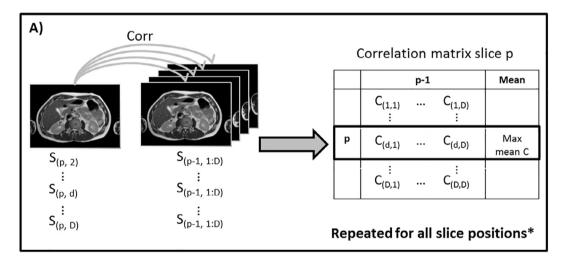
The retrospective self-sorted 4D-MRI method can be split into three parts: acquisition, extraction of the self-sorting signal (SsS) from the image data and reconstruction.

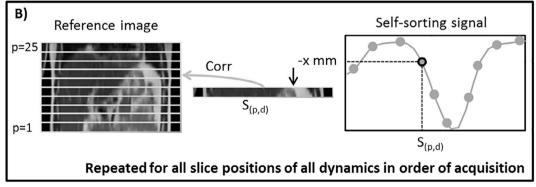
#### Acquisition

A 2D multi-slice single-shot TSE sequence was used (voxels =  $2 \times 2 \times 5 \text{ mm}^3$ , axial slices = 25, SENSE = 2, TE = 60 ms, slice acquisition time = 330 ms, flip-angle = 90°) and repeated a variable number of times (dynamics) D. Slices were acquired in interleaved order, maximizing space and time between every slice acquisition to avoid inter-slice crosstalk and saturation effects. T2-weighting was achieved by imaging the same slice only once per dynamic ( $\sim$ 8 s, i.e. the time to acquire 25 axial slices).

#### Extraction of the self-sorting signal

Liver motion is predominantly cranial-caudal (CC) and this property was utilized to derive a respiratory signal from the images. In the first stage, a (near to) end-exhale reference dataset was extracted from the axial 2D images. As in exhale the liver tissue is in its most cranial position, the anatomy captured in exhale for a given slice position will in other respiratory phases be captured at more caudal slice positions. Therefore, for a given slice position p from every dynamic d, the correlation coefficient with the neighboring caudal slice position p-1 from all dynamics was computed (Fig. 1A). The slice at the given position from the dynamic with the highest average correlation was likely to be acquired in exhale (Fig. 1A). To mitigate variability within the exhale reference dataset, the mean of the two slices with largest correlation was computed and added to the exhale reference image





Slice positions p = 1 ... 25d = 1 ... D

**Dynamics** 

Fig. 1. Extraction of SsS. (A) Slices at position p from all dynamics d are correlated with the neighboring caudal slice  $S_{(p-1,1:D)}$ . The result is a correlation matrix containing the correlation values between p and p-1 from all dynamics. The dynamic N with the highest average correlation is selected for the exhale reference. Step A is repeated for all slice position. For p = 1, the mean of the two slices with the lowest average correlation with p + 1 was selected. (B) All slices S<sub>(p,d)</sub> are correlated to the reference image in order of acquisition, the CC-translations of x mm form the SsS. Note: the interpolation step is not shown for simplicity.

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