Investigation of Internal Target Volumes Using Device and Deviceless Four-dimensional Respiratory Monitoring Systems for Moving Targets in Four-dimensional Computed Tomography Acquisition

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Abstract

Aims and Objectives: The influence of target motion on the reconstructed internal target volume (ITV) for device-based (DB) external surrogate system and Smart deviceless (DL) 4-dimensional (4D) system were compared in a controlled phantom experiment. The volumetric changes in reconstructed ITVs from the average intensity projection (AveIP) images using DB method (Anzai Respiratory Gating System, ANZAI MEDICAL CO., LTD, Japan) and DL method (Smart deviceless 4D system by GE Medical Systems (Chicago, USA)) with the theoretical true volume (ITVth) for moving target with the increasing target motion in anterior-posterior (A-P), lateral (left-right [L-R]) and inferior-superior (S-I) directions were assessed. Materials and Methods: 4D computed tomography (4DCT) of CIRS dynamic phantom (Computerized Imaging Reference Systems Inc., Norfolk, VA, USA) with 2.5 cm diameter spherical target of volume 8.2 cc programmed to move in a cos4(x) motion pattern placed in the lung volume were acquired for various target motion pattern using DB and DL method of gating. AveIP images of 10 phase binned image sets were generated and ITVs were delineated. Results: The maximum absolute percent differences between ITVave and ITVth for DL and DB methods were 15.91% and 4.94 % respectively for target motion of 5 mm in AP with 15 mm S-I direction. When the S-I motion was decreased to 10 mm, the observed % difference of the ITVs were also decreased to 12.5% and 0.3% for DL and DB method. When the lateral [L-R] motion was varied from 0 mm to 5 mm for S-I motion of 5 mm to 15 mm, the differences in the ITVs were significant (P = 0.004) with the maximum absolute percent difference of 18.61% and 4.94 % for DL and DB gating. With the simultaneous motion of the target in all the 3 directions, the difference in the reconstructed ITVs were statistically significant for DL method (P = 0.0002) and insignificant for DB method (P = 0.06) with an average increase of 10% in ITVDL against 2% in the ITVDB. The difference in ITVDL was significant for the target motion above 3 mm in A-P and L-R directions for S-I movement of above 10 mm (P = 0.0002). However, for low excursions of the target movement, no significant difference in the ITVs were observed (P > 0.06). In general, ITVDLs were closer to the ITVth (within 7.8%) than ITVDL (18.61%). Conclusion: The results showed that the DL method is an effective way of image sorting in 4D acquisition for smaller target excursion. When the target motion exceeds 3 mm in A-P and L-R directions with S-I more than 10 mm, DB method is the choice due to its accuracy in reproducing the absolute target volume.

Keywords: 4D CT, ANZAI, device-less 4D, external surrogate, gated radiotherapy, ITV, respiratory monitoring system

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Introduction

Involuntary organ motion like respiratory motion during inter- and intrafraction radiotherapy introduced errors in dose delivery by irradiating excess of normal tissue and missing target volume.1-5 Some of the strategies currently used to reduce respiratory motion effects are integration of respiratory motion into treatment planning (geometrical or dosimetric),
forced shallow breathing with abdominal compression, deep inspiratory breath hold, respiratory gating techniques (four-dimensional computed tomography [4DCT]), and tracking techniques. Conventionally, according to the recommendations by International Commission on Radiation Units and Measurements,\(^3\) in order to create the internal target volume (ITV), tumor motion has to be taken into account by adding a specific safety margin (internal margin) around the clinical target volume (CTV). Positioning uncertainties are then added to create the planning target volume (PTV) to deliver the dose clinically. However, this strategy has its own limits.\(^3,4\) For tumors with significant respiratory motion, such as those near the diaphragm, the addition of various geometric margins leads to irradiation of a large volume of healthy tissue, increasing the risk of complications, and therefore, limiting the possibility of dose escalation.\(^4,6\)

Gated scan allows selected portion of the breathing waveform to be reconstructed, between specified time intervals, or specified amplitudes and dose delivery in a specified portion of the breathing cycle, thus reducing tumor movement when the beam is on. In the presence of the respiratory motion, gated radiotherapy has potential to reduce the size of CTV and PTV by assessing the extent of tumor motion over one respiratory cycle with monitoring the patient’s respiratory motion through an external surrogate.\(^7\)

4DCT creates separate CT images at discrete phases of the respiratory cycle,\(^8\) which allows to see volumetric changes over time. This is achieved by acquiring data at all phases of the respiratory cycle for every table position using continuous scanning in axial cine mode. External surrogates, such as the strain gauge system\(^9,6,10\) are used for synchronous quantification of the abdominal motion during CT acquisition. Projection data are acquired over the duration of the patient’s respiratory cycle plus the duration of one full gantry rotation. Multiple images are then reconstructed per table position and evenly distributed over the acquisition time.\(^11\) Each of the images collected at different anatomical states of the breathing cycle is binned into phase or amplitude of breathing signal. Since patients do not breathe regularly, there is no perfect relation between phase and amplitude. Moreover, respiratory signals obtained from these external surrogates may not always accurately represent the internal target motion, especially when irregular breathing patterns occur.\(^1\) Motion compensated images can also be generated by combining the phases of 4DCT that have been deformed to the same reference state using deformable image registration (DIR).

Artifacts in the 4DCT will directly affect the planning CT and have an influence on the gross tumor volume or ITV. One way to reduce these artifacts is to apply motion compensation to the 4DCT frames since the newer CT systems are having the ability to generate maximum intensity projections (MIPs), average intensity projections (AveIP), and minimum intensity projections by merging several CT series at different phases. MIPs were in use for a long time for target volume delineation since they show a volume which is defined by the tumor’s maximum excursion.\(^11,12\) The ITVs are compared more directly through the contours drawn on MIP images than on phase images since they are more prone to the artifacts.\(^1\) The more recent studies show that more robust 3D planning CT can be created which is less susceptible to respiration artifacts by registering all frames to the time-weighted average position and taking the median or mean over time (mid-position) to generate AveIP.\(^14\)

In 4DCT, the method of extracting the respiratory signals for slice sorting is broadly divided into two categories. One which uses the external signals recorded by extra instruments beside the CT scanner (external motion tracking) and the other one, directly extracts the respiratory signals from the axial CT images (internal motion tracking or data driven). The internal motion tracking uses four features in the cine images whose value was expected to track with the respiratory signal: body area, lung area, air content, and lung density.\(^15,16\) The concept of internal motion tracking has been implemented as Smart Deviceless 4D from GE Medical Systems (Chicago, USA). The product uses additional two features, the physical extent of the lung contour (“lung extension”) and the ratio of the lung area to the body area (“lung-body proportion”). The approximate anatomical location of the current couch position is determined by a feature called lung-body proportion. Except lung-body proportion, all the above features are used to make a respiratory signal at each detector row and couch position. There are several studies evaluating the technical aspects of various gating techniques.\(^17-19\) These studies were mainly limited to the evaluation of technical factors, namely time resolution, signal amplitude, noise, signal-to-noise ratio, signal linearity, and trigger compatibility.\(^17\) For example, when the Siemens CT with external surrogate system (Anzai Respiratory Gating System, Anzai Medical Co., Ltd, Japan) was simultaneously used with optical camera system on a dynamic phantom, tumor trajectories had discrepancies up to 9.7 mm among them.\(^18\) Furthermore, simultaneous use of Varian’s Real-Time Position Management and Anzai Respiratory Gating System resulted in mismatch of gating window with each other due to the discrepancy in breathing traces acquired by the two different surrogate systems.\(^19\) In the absence of a thorough investigation to study the influence of these technical factors on the reconstructed target volumes with statistical inferences, a well-designed, controlled study, directly comparing DB method and DL method with the ground truth volume for 4D sorting, is necessary. The current studies on 4DCT do not include the controlled variations in the breathing pattern including the target motion in all the three directions.\(^17,20,13\) Hence, in this study, we assessed the influence of target motion on the reconstructed target size for DB method (Anzai Respiratory Gating System, Anzai Medical Co., Ltd, Japan) and DL method (Smart Deviceless 4D system by GE Medical Systems, Chicago, USA) in a controlled phantom experiment with the programmed target motion.
The volumetric changes in reconstructed ITVs from the AveIP images using DB method with DL method for moving target with the increasing target motion in antero-posterior (A-P), left-right (L-R), and inferior-superior (S-I) directions were assessed. Results from this work can be used to support the selection of external surrogate against a Smart Deviceless 4D technique based on the patients’ breathing pattern and the extent of target movement which is important for the treatment of small tumors in lung or stereotactic body radiation therapy.

Materials and Methods

Gating methods
The two respiratory monitoring systems for 4DCT acquisition of the moving targets used in this study were Anzai Respiratory Gating System (AZ-733V, Anzai Medical Co., Ltd, Japan) and Smart Deviceless 4D (GE Medical Systems, Chicago, USA). The Anzai Respiratory Gating System consists of an elastic fixation belt and a pressure transducer which is used to quantify the patient’s breathing by positioning it at the patient’s abdomen. During breathing, the fixation belt expands and contracts, and the pressure transducer delivers a digital signal which is processed by the Anzai software (Anzai Medical Co., Ltd, Tokyo, Japan) version 3.8. The system includes two pressure transducers (low/high) with different sensitivities for patients with shallow and deep respiration amplitudes, as well as four different sized fixation belts used to compensate different circumferences of individual patients.\(^\text{[13]}\) The fixation belt with a pressure transducer works as an external surrogate during CT acquisition and treatment thereafter.

The Smart Deviceless 4D option in the Optima 580W CT scanner (GE Medical Systems, Chicago, USA) creates 4D images without the use of an external monitoring device for quantification of the breathing. Deviceless 4D measures internal parameters directly from the patient’s anatomy for an understanding of breathing-induced motion. This option is built into the CT scanner and it offers a simple solution with maximum patient comfort to generate 4D images for use in treatment planning. This system creates 4D images using three main steps: They are follows:

Monitor scan
This is performed to determine the patient breathing pattern and respiratory period.

While performing a monitor scan, a short metal wire marker (lead wire of about 5 cm length) was placed on the patient’s abdomen at the position of maximum breathing amplitude. Two scout projections at 0° and 90° were executed, and the middle position of the wire marker in both z-axis (in and out planes of the couch translational motion) and y-axis (A-P of the couch translational motion) was identified. The z-position was used to recommend a scan start position for the monitor scan, and the y-position was used to help initiate motion tracking.

Once three consecutive stable periods for the middle positions were detected, the collected data will be displayed. This includes the calculated minimum, maximum, and the average breathing period.

Cine acquisition
Cine scan parameters were transferred into the protocol based on the results of the monitor scan. Successful 4D imaging requires the data collection at every scan location for the entire duration of the patient’s breathing cycle. To ensure a complete breathing cycle, an additional time of one gantry rotation was added to the average breathing period for the cine scan.

Collecting scan data for less than the respiratory period can result in undersampling and therefore artifacts in the eventual 4D image set. At this point, the breathing curve signal from the body area, lung area, air content, lung density, lung extension, and lung-body proportion undergoes a postprocessing step to extract the key waveform properties such as breathing period, peak (0% phase) location, and valley (50% phase) location for each scan location. The waveform extraction was performed in the frequency domain through a fast Fourier transform of the amplitude measurements of the breathing curves. Once the breathing period, peak location, and valley location are identified, a simple linear extraction was performed to determine the phase position of each image in the cine data.

Image processing
Cine CT scan data were processed using the D4D algorithm (GE Medical Systems, Chicago, USA) to generate AveIP from the 4D dataset.

Dynamic Thorax phantom with moving target
The Dynamic Thorax Phantom model 008A (CIRS, Norfolk, VA) with CIRS motion control software [CIRS, Norfolk, VA, USA] (version 2.4.0) was used in this work. This phantom contains a 2.5-cm diameter spherical target of volume 8.2 cc placed inside the lung volume. The target with the surrogate was independently controlled with CIRS motion control software by applying various amplitude, cycle time, and phase shifts.\(^\text{[12]}\)

The true volume of the target was measured by contouring the gross tumor volume on static CT images of the dynamic phantom. Volume measurement precision was quantified by calculating the coefficient of variation (COV) for the five replicate volume measurements in five sets of CT images. The measured COV for the target volume was within 1.7% of the true physical volume which was well within the upper limit on volume measurement accuracy for small target volumes.\(^\text{[20]}\) Then, the target in the phantom was programmed to execute ± 5 mm, ±10 mm, and ± 15 mm excursions in the S-I direction about their corresponding reference positions. In addition to programmed S-I motion, by choosing appropriate simultaneous rotation about the longitudinal axis (S-I), clinically realistic tumor motions in both the A-P and L-R directions were programmed from ± 0 mm to ± 5 mm with 1 mm increment, respectively. The programmed 3D motion amplitudes were selected to reflect clinically relevant tumor motions commonly observed for pulmonary lesions. Motion cycle period was set to 5 s, consistent with typical human
breathing cycles. The external surrogate was programmed for ±10 mm excursions representing normal respiration of the patients. CT scans were performed for a target in dynamic mode (target undergoing 3D motion involving simultaneous S-I, A-P, and L-R displacements). Clinically realistic patient breathing cycles with a nonconstant amplitude and periodicity were approximated by the COS² model.[22]

**Four-dimensional computed tomography acquisition**

Cine CT images of 0.625-mm slice thickness were acquired with the tube current of 200 mA and voltage of 120 KVp. The gantry rotation time was kept at 0.8 s per rotation for all the acquisitions. Respiratory signals were acquired for the DB method using the surrogate-based Anzai system (AZ-733V) for all the target excursions simultaneously during the CT scans. The same was repeated for DL method. The scan time at each table position was set to ensure that the scan covers the entire respiratory cycle per table position. The raw CT data were sorted and reconstructed using a phase binning reconstruction based on the respiratory profile provided by the Anzai system (DB method) and deviceless system (DL method). AveIP images were generated using 10 phase-binned image sets since the amplitude in our study was less than 3 cm.[23] AveIP images were used in our study because of their importance in creating contours in the clinical practice and to avoid the additional complexity of contouring each phase.[14] The AveIP images were exported to Monaco (version 5.10) treatment planning system (Elekta, Crawley), and the ITV delineation was done with a consistent window width of 600 and window level of 40.

**Theoretical internal target volume**

For comparing the segmented ITV volume from the AveIP, a theoretical ITV (ITV_{th}) was calculated for all the tumor excursions. For a tumor with radius “r," if “L” is the tumor excursion in S-I, A-P, and L-R directions within the gating window, the volume of the shape comprising a sphere plus a cylinder with the same radius was approximated by the equation:

\[
\text{ITV}_{\text{th}} = \left(3\pi r^3\right)/4 + \pi r^2 L_{\text{A-P}} + \pi r^2 L_{\text{L-R}} + \pi r^2 L_{\text{S-I}} \quad \text{EQ (1)}
\]

“L” can be deduced from the programmed sequence at CIRS phantom in S-I, A-P, and L-R directions.

**Results**

The ITVs for target motion in S-I, A-P, and L-R directions generated using DB and DL methods were analyzed for percentage difference with the ground truth volume calculated as per EQ (1).

**Target motion in anterior-posterior and inferior-superior directions**

The target motion ranging from 0 to 5 mm in increment of 1 mm was introduced in A-P direction with a simultaneous motion of 5, 10, and 15 mm in S-I direction. The left-right (L-R) motion of the target was kept at zero, and the surrogate excursion was kept at 10-mm amplitude. The 4DCT acquisitions were made with both the techniques of respiratory gating. The AveIP images with 10 phase bins were reconstructed, and ITV was contoured as ITV_{ave} and ITV_{db} from DL method and DB method AveIP images. These ITVs were evaluated to determine the change in volume with respect to the theoretical volume calculated as per EQ (1).

When the target motion in A-P direction ranged from 0 to 5 mm and 5, 10, and 15 mm in S-I direction for a fixed surrogate amplitude of 10 mm, the ITV varied from 11.4 to 21.1 cc for DL method, whereas it varied from 10.9 to 18.9 cc for DB method. The maximum absolute percentage difference of ITV_{ave} with the ITV_{ave} for DL and DB methods was 15.91% and 4.94% for target motion of 5 mm in A-P and 15 mm in S-I directions. When the S-I motion was decreased to 10 mm, the observed percentage difference of the ITVs was also decreased to 12.5% and 0.3% for DL and DB methods.

This was further subjected to a statistical test with the hypotheses of (H0: \(\mu_1=\mu_2\)) for the mean volume (\(\mu\)) of ITV among true volume and DL and DB methods. For the motion of combination of the target in a-P = 0–5 mm, S-I = 5 mm, and surrogate = 10 mm, the differences in ITVs of DL and DB methods with true volume was statistically not significant (\(P = 0.129\)) at confidence level of 95% (\(\alpha = 0.05\)) for method. For the target motion in S-I direction above 5 mm with A-P direction above 3 mm, the differences in ITVs were statistically significant (\(P < 0.003\)) for DL method. However, for ITV_{ave} the volume change was not significant for the same motion combination in A-P and S-I directions (\(P = 0.43\)).

**Target motion in left-right and inferior-superior directions**

In this case, the L-R motion ranging from 0 to 5 mm with a fixed movement of 10 mm in the surrogate was introduced with A-P motion fixed at zero. The S-I motion ranging from 5 mm to 15 mm dimension was introduced. ITV was generated from the AveIP images of 10 phase bins. ITVs were evaluated to determine the change in volumes with ITV_{ave} to ITV_{ave} and ITV_{ave} systems. When the left-right (L-R) motion was varied from 0 to 5 mm for S-I motion of 5–15 mm, absolute volume of the delineated ITV changed from 11.3 to 21.2 cc for DL system and 10.9 to 18.9 cc for DB system against true volume of 10.63–17.99 cc. The maximum absolute percentage difference of ITV_{ave} with the ITV_{ave} for DL and DB gating volume was 18.61% and 4.94% for target motion of 5 mm in L-R and 15 mm in S-I directions.

The ITVs were overestimated by the DL method as the L-R motion for the target was increased above 3 mm (\(P = 0.004\)) with the S-I motion of 10 and 15 mm. As the L-R motion decreased below 3 mm with S-I motion of 5, 10, and 15 mm, the change in ITV volume was not significant (\(P = 0.69\)).
ITV\textsubscript{DB} did not vary significantly as the motion in L-R direction increased above 3 mm with the S-I motion of 5-, 10-, and 15-mm dimension ($P = 0.23$). Figure 2 represents the ITV\textsubscript{th} calculated using the EQ (1), the ITV from DB and DL method with their respective motion pattern in S-I and L-R directions.

**Simultaneous motion of the target in S-I, A-P, and L-R directions**

Target motion in all the three directions with A-P ranging from 0 to 5 mm, L-R ranging from 0 to 5 mm, and S-I ranging from 5 to 15 mm dimension was introduced. The surrogate amplitude was fixed at 10 mm. The generated ITVs showed an increase in the volume from 14.06 to 24.3 cc for DL method against 13.08–20.44 cc of the true volume with the maximum percentage difference of 18.3%. For DB method, the increase in the volume was from 13.25 to 22.1 cc with the maximum percentage difference of 7.8% for movement of 5, 5, and 15 mm in A-P, L-R, and S-I directions. The difference in the reconstructed ITVs was statistically significant for DL method ($P = 0.0002$) and insignificant for DB method ($P = 0.06$). In general, the average increase in the ITV\textsubscript{DL} was 10% against 2% by DB method. However, this increase turned significant as the target motion increased above 2 mm in A-P and L-R directions for S-I movement of 5, 10, and 15 mm. The average increase in the ITV volume for motion in A-P and L-R directions above 2 mm was 15.6% and 5% for DL and DB method [Figure 3].

**Discussion**

The present work focused on the difference in the target volume generated from the AveIP images reconstructed from DB and DL methods in the presence of target motion in S-I, A-P, and L-R directions. In this study, we intended to compare the DB method and DL method of 4DCT sorting with the theoretical true volume of the target motion. It was necessary to produce a comparative study to ensure differences of the two gating systems with the true volume for accurate planning and treatment. The assumption of this study was that there would be a good correlation between

![Figure 1: The internal target volumes generated from average intensity projection images acquired at fixed surrogate of 10 mm with inferior-superior motion ranging from 5 to 15 mm and anterior-posterior motion ranging from 0 to 5 mm for DL and DB methods with their theoretical volume. The values in the parenthesis represent the dimension of the motion in inferior-superior and anterior-posterior direction in mm](image1)

![Figure 2: The variation of internal target volumes generated from average intensity projection images acquired at fixed surrogate of 10 mm with inferior-superior movement ranging from 5 to 15 mm and left-right (L-R) motion ranging from 0 to 5 mm for DL and DB methods with their true volume calculated (ITV\textsubscript{th}). The values in the parenthesis represent the dimension of the motion applied in inferior-superior and left-right direction in mm](image2)
the tumor volume and the external surrogate or lead marker motion. Furthermore, this correlation would be consistent over the entire course of the treatment. This was achieved with the help of the CIRS dynamic phantom with target motion in known dimensions. Several studies demonstrated a good correlation between external marker motion and internal organ movement in free-breathing respiratory gating treatment.\[6,10,17\] ITV generated from deviceless 4D gating AveIP images systematically showed higher volumes for the moving target compared to the DB method. This difference was evident as the motion in A-P, L-R, and S-I directions increased [Figure 4]. This could be due to large physical amplitude separation from a particular phase point in the respiratory cycle due to fast respiratory motion and the virtual interpolation applied to account for potential phase mismatch between couch positions in the Z-direction by the D4D algorithm. For fast respiratory movement, two images may be close in phase but have a large difference in physical amplitude resulting in a visible error in the sorted 4D data. When this happens, an amplitude binning approach is applied to identify an available image at the couch position that will best meet the target criteria making an approximation.

The percentage difference of ITV generated from DL method increased for higher variability of S-I, A-P, and L-R target motion. The difference in the ITVs was not significant for combination of motion in S-I and A-P directions with the dimensions <10 and 0–5 mm, respectively. However, when the motion in S-I direction increased to 10 mm or more, the differences in the ITVs were significant for motion in the A-P direction above 3 mm. These observations suggest the use of Smart Deviceless 4D gating option for the patients with shallow breathing patients with target motion up to 10 mm in the S-I direction with A-P motion up to 5 mm with external surrogate motion of 10 mm. Similarly, when the motion in the L-R direction was increased to 3 mm or above, the differences in the ITVs were significant ($P = 0.004$) for DL method. When the motion was applied simultaneously in all the three directions, the reconstructed ITVs for DL method was significantly larger ($P = 0.0002$). Further, our observations showed that the Anzai system introduces a nonlinear dependency between the actual motion and the measured signal, mainly caused by elasticity of the rubber fixation belt causing an additional error. The magnitude of this additional error was hardly predictable and depends on the fixation belt and the applied forces. While using the deviceless 4D, the initial monitor scan requires and assumes the regular breathing and respiratory period of the patient for the entire scan duration which is far from reality. This assumption can cause irregular breathing motion artifacts which can be reduced in prospective gating systems like the DB method used in this study. The prospective gating systems limit the 4DCT “beam-on” time to regular breathing, defined in terms of real-time displacement, velocity, and/or phase criteria. The 4DCT image artifacts due to irregular breathing pattern impact even the accuracy of DIR results. To overcome this problem, 4D DIR was proposed which may smooth out some artifacts using temporal regularization.\[24\] In our study, this was overcome using the regular breathing pattern in the CIRS phantom. Although DIR addresses many problems associated with 4DCT, at the present time, majority of radiotherapy clinics are using only rigid registration at treatment planning and delivery. Even when deformable registration is available for use, regardless of the algorithm chosen, limitations and challenges remain. For example, the algorithms in DIR use a model to describe the deformation such as smoothness of the vector field which may lead to registration error when singularity of the vector field exists.\[25\] Another limitation of this study is the fact that the basic image acquisitions were not simultaneously carried out for both the techniques of gating. This was due to the technical limitation of the acquisition software (Advantage 4D version 2.3.104) at Optima 680 (GE Medical Systems, Chicago, USA) CT scanner.

**Conclusion**

In clinical practice, the combination of a GE CT scanner and the Anzai belt system will provide better results in 4DCT reconstruction for the breathing patterns of the patients with high excursions due to the compatibility of methods in
image sorting (CT) and respiratory monitoring system. The differences in the reconstructed ITVs were observed while using deviceless 4D in phantom for target motion with high excursions (S-I above 10 mm, L-R above 3 mm, and A-P above 3 mm for surrogate motion of 10 mm). However, for low excursions of the target motion, deviceless 4D method is ideal due to its simplicity and user-friendliness.

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Conflicts of interest
There are no conflicts of interest.

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