Introduction of a novel ultrahigh sensitivity collimator for brain SPECT imaging

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Purpose: Noise levels of brain SPECT images are highest in central regions, due to preferential attenuation of photons emitted from deep structures. To address this problem, the authors have designed a novel collimator for brain SPECT imaging that yields greatly increased sensitivity near the center of the brain without loss of resolution. This hybrid collimator consisted of ultrashort cone-beam holes in the central regions and slant-holes in the periphery (USCB). We evaluated this collimator for quantitative brain imaging tasks.

Methods: Owing to the uniqueness of the USCB collimation, the hole pattern required substantial variations in collimator parameters. To utilize the lead-casting technique, the authors designed two supporting plates to position about 37 000 hexagonal, slightly tapered pins. The holes in the supporting plates were modeled to yield the desired focal length, hole length, and septal thickness. To determine the properties of the manufactured collimator and to compute the system matrix, the authors prepared an array of point sources that covered the entire detector area. Each point source contained 32 μCi of Tc-99m at the first scan time. The array was imaged for 5 min at each of the 64 shifted locations to yield a 2-mm sampling distance, and hole parameters were calculated. The sensitivity was also measured using a point source placed along the central ray at several distances from the collimator face. High-count projection data from a five-compartment brain phantom were acquired with the three collimators on a dual-head SPECT/CT system. The authors calculated Cramer-Rao bounds on the precision of estimates of striatal and background activity concentration. In order to assess the new collimation system to detect changes in striatal activity, the authors evaluated the precision of measuring a 5% decrease in right putamen activity. The authors also reconstructed images of projection data obtained by summing data from the individual phantom compartments.

Results: The sensitivity of the novel cone-beam collimator varied with distance from the detector face; it was higher than that of the fan-beam collimator by factors ranging from 2.7 to 162. Examination of the projections of the point sources revealed that only a few holes were distorted or partially blocked, indicating that the intensive manual fabrication process was very successful. Better reconstructed phantom images were obtained from the USCB+FAN collimator pair than from either LEHR or FAN collimation. For the left caudate, located near the center of the brain, the detected counts were 9.8 (8.3) times higher for UCSB compared with LEHR (FAN), averaged over 60 views. The task-specific SNR for detecting a 5% decrease in putamen uptake was 7.4 for USCB and 3.2 for LEHR.

Conclusions: The authors have designed and manufactured a novel collimator for brain SPECT imaging. The sensitivity is much higher than that of a fan-beam collimator. Because of differences between the manufactured collimator and its design, reconstruction of the data requires a measured system matrix. The authors have demonstrated the potential of USCB collimation for improved precision in estimating striatal uptake. The novel collimator may be useful for early detection of Parkinson's disease, and for monitoring therapy response and disease progression. © 2016 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4958962>]

Key words: high sensitivity brain SPECT, collimator design, DAT imaging, Parkinson's disease

1. INTRODUCTION

1.A. Brain SPECT

There is a critical need for valid biomarkers of Parkinson's disease (PD); in particular, there is great interest in developing biomarkers that would make it possible to diagnose the disease well before clinical symptoms appear.¹ A multicenter clinical study, The Parkinson's Progression Markers Initiative, is in progress with the goal of validating biomarkers; among these are imaging biomarkers, including those based on single-photon emission computed tomography (SPECT) imaging of the striata. Dopamine transporter (DAT) imaging has been recognized as a "lead PD biomarker candidate."² Longitudinal changes in striatal DAT density are being evaluated as endpoints in clinical trials of PD therapy,³ and functional striatal volume has also been proposed as a marker of disease status.⁴ Working against the successful development of SPECT-based biomarkers for PD is the fact that, because of photon attenuation, standard SPECT imaging systems are least sensitive to structures, such as the striata, that are located near the center of the brain. For a number of years we have worked to improve the sensitivity of SPECT imaging systems to these deep structures, and we have been able to accomplish this without loss of spatial resolution and without loss of sensitivity to peripheral brain regions. Furthermore, our solution does not require redesign of the SPECT system, but only replacement of a relatively inexpensive component, the collimator.

SPECT imaging is most frequently accomplished using parallel-hole collimation, which yields uniform count sensitivity and spatial resolution across the detector. Photons emitted from structures deep in the brain (or body) are preferentially attenuated, leading to inaccurate activity estimation and high noise levels in these regions of the reconstructed images. Attenuation correction algorithms correct the bias due to this effect, but they cannot improve the precision. We have previously shown that this problem can be addressed by nonuniform transaxial sampling of the projections, with central regions more heavily represented, in order to compensate for loss of information from central brain structures by attenuation.⁵ Centrally peaked collimator sensitivity can yield improved precision, particularly in central regions, without degrading spatial resolution. There are several ways to achieve centrally peaked collimator sensitivity. We have previously designed and evaluated a collimator for a dedicated brain system (CeraSPECT, Digital Scintigraphics, Inc.) with cylindrical geometry that accepts more photons from the central region than from the periphery.⁶ The new collimator led to substantially improved detection and estimation performance throughout the brain. We have also assessed the potential of a SPECT system with adaptive data acquisition (D-SPECT, Spectrum Dynamics, Caesarea, Israel) for brain imaging.⁷ The results of this analytical study implied that the increased sensitivity of the D-SPECT over the conventional system would lead to significantly improved performance in estimating clinically important metrics, such as striatal uptake, binding ratio, and the left-right asymmetry index. A third approach to achieving centrally peaked collimator

sensitivity, compatible with standard dual- or triple-head SPECT systems, is to use converging collimation, i.e., fan- or cone-beam geometry; maximum sensitivity is achieved for a source at the focal point or along the focal line. There have been many previous efforts to increase sensitivity with various fan- and cone-beam designs;^{8,9} however, the sensitivity gains were limited by the need to maintain a large field of view, the need to avoid the shoulders, and the hole angle constraints imposed by conventional collimator manufacturing techniques. In all of these designs, the focal lengths are greater than 40 cm and, therefore, outside the brain; consequently, the potential for increased sensitivity is not fully exploited.

We have previously shown that a cone-beam collimator with a very short focal length can lead to substantial gains in sensitivity for brain SPECT.¹⁰ Our approach was to pair an ultrashort-focus cone-beam (USCB) collimator, with focal point inside the brain and shifted caudally for shoulder clearance, with a conventional fan-beam collimator to ensure data sufficiency. For brain imaging with a 15-cm radius of rotation, the focal point of the USCB with $f = 20$ cm is located near the center of the brain, where the maximum sensitivity is achieved. In computer simulation experiments, the sensitivity of the USCB was ~ 10 times higher at the center of the brain than that of a low-energy high-resolution (LEHR) parallel collimator. A similar approach has been developed to increase the detected number of photons for cardiac SPECT imaging using a variable focus collimator.¹¹

For this study, we designed and manufactured a USCB collimator, evaluated it for quantitative brain imaging tasks, and compared it to LEHR and 39-cm-focal-length fan-beam (FAN) collimation on the basis of performance in quantitative imaging tasks. Our performance metric is a signal-to-noise ratio (SNR) based on the Cramer-Rao bounds (CRB) on precision of estimating the parameters of interest. Our approach differs from that of others who use CRB-based imaging system assessment in that we model the image in terms of a relatively small number of unknown parameters, rather than calculating bounds on all voxel values in the image dataset. CRB on voxel values are extremely difficult to calculate because of the need to invert very large matrices. In this study, the unknown parameters are the (assumed uniform) activity concentration values within four striatal structures and the background. This methodology, which we have used previously,⁷ is analogous to the well-established mathematical observer approach which is standard in detectability studies, i.e., performance is assessed using a prototypical imaging task. The CRB are lower bounds on the variance with which these unknown parameters can be estimated by an unbiased estimator. Our quantitative task-based metric is a SNR defined as the true parameter value divided by the square root of the CRB.

We measured the system matrix of the new collimator in order to assess the accuracy of the manufacturing process and as a basis for the reconstruction algorithm. We generated tomographic images of the striatal phantom, reconstructed from the USCB+FAN collimators, as well as from LEHR and FAN collimation.

FIG. 1. Design of the novel ultrashort cone-beam (USCB) collimator, (a) detector side of the collimator, (b) coronal view showing the collimator configuration for a brain SPECT acquisition using USCB and FAN collimators, and (c) transaxial view, indicating the differing focal lengths of the USCB and FAN collimators.

2. METHODS

A hybrid design was required for the USCB collimator because of the short focal length and the limit on hole angle that can be achieved using lead casting. The original design we presented in Fig. 1 of Ref. 10 has been modified to include a slant hole region. The cone-beam holes, focused at 20 cm from the surface of the collimator, fill the central area of the collimator [Fig. 1(a)]. The slant holes, which are also located in a radially symmetric pattern, are at 37.7° to the normal to the collimator surface; therefore, the focal length in the slant region varies with distance from the hole to the focal axis. For shoulder clearance, the focal point was shifted down caudally by 10 cm [Fig. 1(b)]. The collimator face was 53×39 cm, and the diameter of the central cone-beam section was 36.4 cm. Hole length, hole size, and septal thickness varied with position on the detector face, as illustrated in Fig. 2.

The USCB collimator was manufactured by Nuclear Fields USA (Des Plaines, IL) using pin guidance plates specified by the BWH physics group; this was challenging because the profiles of $\sim 37\,000$ pin intersections with the two guide plates depended on angle, which varied with distance from the focal axis. Septal thickness on the entrance face ranged from 0.24 mm near the focal axis to 0.4 mm near the edge of the

focal section and thickness increased with distance below the entrance surface because of the angulation of the pins. We used hexagonal steel pins with a fixed size. The pins were slightly tapered from one end to the other. Because of the focusing design, the distance between pins varies. Furthermore, the cross-sections of the hexagonal holes parallel to the collimator surfaces are elongated, and the degree of elongation varies with distance from the focal axis. We specified two plates to hold the pins, with openings for each pin corresponding to its elongated cross-sections at the levels of the two faces of each of the two plates, in order to yield the desired focal length.

We prepared computer files specifying the hole configurations for each plate using a computer-aided design (CAD) software package (Solidworks, Waltham, MA). The plates were fabricated by photoetching, guided by the CAD files, and used to position the steel pins in the specified locations and orientations to form the cone-beam and slanted holes. Each of the $\sim 37\,000$ steel pins was positioned manually through the matching holes on the two plates (Fig. 2). From this point, lead casting proceeded as for parallel-hole collimators. Molten lead was poured between the plates, and all pins were carefully removed after cooling. Both entrance and exit surfaces of the collimator were polished to yield the desired collimator thickness (37 mm); hole length varied from 37 mm near the focal axis to 46.8 mm near the edge of the cone-beam section. Nuclear Fields also manufactured a standard fan-beam collimator that was optimized for I-123 imaging. The design parameters for both fan- and cone-beam collimators are summarized in Table I along with those of a low-energy high-resolution collimator. Gunter *et al.*¹² pointed out that the optimization of hole parameters for a nonparallel hole collimator is similar to optimization for a parallel hole collimator, as adjacent holes are virtually parallel. It should

FIG. 2. Manufacturing setup of the USCB collimator.

TABLE I. Parameters for the collimators used in this study.

Parameters	LEHR	FAN	USCB
Hole size (mm)	1.11	1.5	1.46
Septa (mm)	0.16	0.23	0.24
Hole length (mm)	24.05	34.9 ^a	37 ^a
Focal length (mm)	NA	390	200

^aAt location of the perpendicular ray through the focal point.

be noted that the FAN and USCB collimators were both designed to be useful for imaging I-123 and, in particular, the USCB average septal thickness and hole length are larger than those of the FAN, and substantially larger than those of the LEHR collimator. By computing a weighted average of the single-septal penetration (SSP) fraction over all I-123 decay-photon energies, we determined that the SSP through the USCB would be <2%. The USCB collimator also weighs 50% more than the FAN collimator, which had also originally been designed for I-123 imaging (62 vs 41 kg). This provides an additional indication that the septal penetration and scatter from the USCB collimator when imaging either I-123 or Tc-99m should be significantly less than those from the FAN collimator. Even with the weight imbalance between two heads, the detector sagging and tilt were too small to measure; therefore, no physical or mathematical adjustment was applied.

The USCB collimator is mounted on one head of a Siemens Symbia T6 SPECT/CT scanner (Siemens Medical Solutions USA, Inc., Knoxville, TN) and the conventional 39-cm focal-length fan-beam collimator (FAN) is mounted on the other. The FAN provides complete projection data for simultaneous reconstruction of both cone-beam and fan-beam projections without artifacts.

2.A. Evaluation of holes

A large array of point sources was prepared to determine the properties of the manufactured collimator. 2-mm diameter point sources, each consisting of 32 μCi Tc-99m, separated by 16 mm in both directions, covered the entire detector area (39×53 cm). The array was positioned parallel to the collimator and 1 cm away from its front surface. The array was imaged for 5 min at each of the 64 shifted locations to achieve a sampling distance of 2 mm. We estimated each hole angle and axial offset, based on the relationship between the centroids of the point sources and those of their projections on the detector. We also estimated the coordinates of the center of the FOV of the cone-beam section. These data also made it possible for us to identify any holes with imperfections and to locate the boundary between cone and slant holes.

2.B. Projection-based performance evaluation (CRB)

We acquired projection datasets for all three collimators, LEHR, USCB, and FAN, using the RSD striatal phantom (Radiology Support Devices, Long Beach, CA). The phantom consists of five separately fillable compartments for left and right caudate and putamen and brain background. One compartment at a time was filled with radioactive Tc-99m solution, while the other compartments were filled with water. The activity concentration at the time of the scans ranged from 45 to 65 $\mu\text{Ci/ml}$ for the striatal compartments and from 2 to 3 $\mu\text{Ci/ml}$ for the background. After each filling, the phantom was placed on a head-holder and positioned in the scanner, using the built-in laser lines to ensure that the phantom was in the same position for each scan.

Each projection dataset consisted of 60 angular views per detector over a 360° step-and-shoot circular orbit; acquisition time was 90 s/view. The radius of rotation was 13 cm.

All acquisition data were scaled to count levels expected for unit activity concentration, 1 $\mu\text{Ci/ml}$, so that we could compare detected counts for each collimator. From the normalized projection data, we calculated the Cramer-Rao lower bounds (CRB)¹³ on the precision of estimates of striatal and background activity concentration.

The CRB are independent of the estimation method, and they represent the theoretically optimal performance for an unbiased estimator. This approach implicitly incorporates the effects of scatter and attenuation, as well as spatial resolution and sensitivity. The CRB are obtained by inverting Fisher's information matrix, which can be calculated from the projection data. Note that although we calculated the CRB from the projection datasets, they also constitute bounds on estimation performance from images reconstructed from these datasets, because they are based on the full information content of the acquired data. An advantage of this projection-based approach is that the metrics reflect the fundamental properties of the imaging systems (including collimation) without being confounded by the properties of the reconstruction algorithm. Our calculations were based on the following model:

$$I(\theta, x, y) = A_{rp}P_{rp}(\theta, x, y) + A_{lp}P_{lp}(\theta, x, y) + A_{rc}P_{rc}(\theta, x, y) + A_{lc}P_{lc}(\theta, x, y) + A_bP_b(\theta, x, y), \quad (1)$$

where $P_{rp}(\theta, x, y)$, $P_{lp}(\theta, x, y)$, $P_{rc}(\theta, x, y)$, and $P_{lc}(\theta, x, y)$ are the projections of the right and left putamen and caudate at pixel position (x, y) on each detector and at angular view θ . $P_b(\theta, x, y)$ is the projection of the background, which includes the rest of the brain. A_{rp} , A_{lp} , A_{rc} , and A_{lc} are the activity-concentration values in the four striatal compartments, and A_b is the activity concentration in the background; activity concentrations were assumed to be uniformly distributed within each compartment. The 5×5 Fisher's information matrix (FIM), J , was calculated from the projections by

$$J_{ij} = \sum_{\det} \sum_{\theta, x, y} \left[\frac{\partial I(\theta, x, y)}{\partial A_i} \right] \left[\frac{\partial I(\theta, x, y)}{\partial A_j} \right] \cdot \frac{1}{I(\theta, x, y)}, \quad (2)$$

where A_i is the activity concentration in compartment i , i.e., right putamen ($i = 1$), left putamen ($i = 2$), right caudate ($i = 3$), left caudate ($i = 4$), and background ($i = 5$) for our study. The entries of the FIM were summed over all detector pixels, all projection angles, and the two detector heads; all quantities were evaluated at the true values of the striatal and background activity concentration. The diagonal entries of the inverse of FIM are the CRB on the variance of activity-concentration estimates in the five compartments. Therefore, we define the task-specific ideal-estimation signal-to-noise ratios for measuring activity concentration within the striatal compartments by

$$\text{SNR}_{rp} = \frac{A_{rp}}{\sqrt{J_{11}^{-1}}},$$

FIG. 3. Point source array projected on (a) LEHR and (b) USCB collimator. The three brighter spots (in white circles) on the LEHR projection correspond to higher activity point sources, which were intentionally added in order to aid in identification of the source positions across all 64 collimator images. The same three points are also circled on the USCB projection.

$$\text{SNR}_{\text{lp}} = \frac{A_{\text{lp}}}{\sqrt{J_{22}^{-1}}},$$

$$\text{SNR}_{\text{rc}} = \frac{A_{\text{rc}}}{\sqrt{J_{33}^{-1}}},$$

$$\text{SNR}_{\text{lc}} = \frac{A_{\text{lc}}}{\sqrt{J_{44}^{-1}}}.$$

(3)

In order to assess the potential of the new collimation system to detect changes in striatal activity due to disease progression or response to therapy,¹⁴ we evaluated the precision of measuring a 5% decrease in right putamen activity. The SNR for detecting a change of 5% was given by

$$\text{SNR}_{\Delta 5\%} = \frac{0.05A_{\text{rp}}}{\sqrt{\text{CRB}(A_{\text{rp}}) + \text{CRB}(0.95A_{\text{rp}})}},$$

(4)

An analogous SNR can be defined for estimation of background activity concentration; however, this is usually not of interest.

where $\text{CRB}(*)$ is the CRB on A_{rp} evaluated at $*$.

Finally, we used the measured centroid positions of all points to compute the system matrix that was then used in an

FIG. 4. Point-source response through collimators at several distances (y) from the entrance surface. (A) Projection images of the point source at 10 cm from the collimator surface through all three collimators. (B) Magnified projection images of the point at three distances from the entrance surface through the fan and USCB collimators. The regions of the USCB image at 18 cm that appear to be nonuniform are attributable to small local variations in the collimator-hole angles arising from the manufacturing process; these are not expected to adversely affect the final reconstructed images because the fully nonstationary PSF will be measured and used by the reconstruction algorithm. The large circular ring at $y = 30$ cm for the USCB collimator resulted from photons that went through the slant-hole section.

FIG. 5. Count sensitivity of the three collimators measured using a point source.

OSEM reconstruction of summed data from all compartments of the striatal brain phantom. For 5:1 striatal/background uptake ratio, the summed projection data were created for a dual-head SPECT camera equipped with LEHR+LEHR, FAN+FAN, and USCB+FAN collimators, and reconstructed using threshold-based attenuation compensation along with TEW-based scatter estimates, with six iterations and six subsets.

3. RESULTS AND DISCUSSION

The USCB collimator was inspected for manufacturing imperfections using the 64 shifted images of the large point-source array placed directly on the detector head. The projection of each point source was carefully examined, revealing that fewer than 1% of the holes were imperfect. This indicates that the intensive manual fabrication process was very successful. Projections through the USCB and LEHR collimators with the point-source array placed directly on the detector head (1 cm from the surface) are shown in Fig. 3. Using the known physical location of each point source, we were able to calculate the hole angles within the USCB collimator. Because of the differences between the design and the manufactured collimator, we used the measured point-spread function, rather than the analytical function describing the design, in the reconstruction algorithm.

The sensitivities of the fan-beam and USCB collimators were measured using a Tc-99m point source positioned at the center of the cone-beam section; the distance (y) from the source to the entrance face of the collimator was varied from 9 to 30 cm, the relevant range for most brain SPECT

FIG. 7. Detected counts per angular view for the left caudate filled with 1 $\mu\text{Ci/ml}$ concentration of Tc-99m. The large variations in counts for the USCB collimator correspond to the structure moving toward and away from the highest-sensitivity region as the detectors rotate.

imaging [Fig. 4(B)]. Projections were acquired, and counts were corrected for radioactive decay and summed over all views. The sensitivity was calculated in counts per minute (cpm) per unit activity, $\text{cpm}/\mu\text{Ci}$.

Sensitivity was higher for the USCB collimator than for the fan-beam collimator by factors ranging from 2.7 to 162 for the y-range that we measured (Fig. 5). The sensitivity of a LEHR parallel-beam collimator is 202 $\text{cpm}/\mu\text{Ci}$, constant with distance from the collimator.

In Fig. 6, we show one projection view for each collimator for the left caudate filled with Tc-99m while all other compartments are filled with nonradioactive water. As expected, a larger detector area recorded photon counts for the USCB compared to LEHR and FAN. For this specific angular view, the detected counts were 680, 754, and 3176 for LEHR, FAN, and USCB collimator, respectively.

The detected counts for other angular views of the left caudate were plotted in Fig. 7 for each collimator. For a concentration of 1 $\mu\text{Ci/ml}$ of Tc-99m, the total detected counts, summed over 60 views covering 360° , were 32 930, 39 279, and 283 254 for LEHR, FAN, and USCB, respectively. The projection through the USCB collimator in Fig. 6(c) involves many more holes than projections through the LEHR or fan beam collimator. Photons traveling through the holes away from the central projection have longer path-length; therefore the projection is stretched out and blurry.

For the count sensitivity measurements, background counts were measured for each collimator and subtracted from projected counts of each compartment. For the left caudate,

FIG. 6. One projection view of the left caudate for (a) LEHR, (b) FAN, and (c) USCB.

located near the center of the brain, the detected counts were 9.8 (8.3) times higher for USCB compared with the counts for LEHR (FAN), averaged over 60 views. The gain varied with projection angle, as the USCB focal point moved with respect to the structure (Fig. 7). For the left putamen, the sensitivity of USCB was 6.9 times higher than that of LEHR. The lower gain was expected due to the location of the putamen relative to the focal point of the USCB collimator. The total detected counts summed over 60 views in Fig. 7 were 32 014, 37 947, and 296 912 for LEHR, FAN, and USCB, respectively; therefore, the sensitivity of the combined FAN and USCB acquisition on a dual-head SPECT scanner would be 5.2 times greater than an acquisition equipped with two LEHR collimators.

The ideal-estimation SNR for estimation of striatal activity concentration, in the presence of background activity, is summarized in Fig. 8. All four striatal compartments were at equal activity concentration, five times greater than that of the background. The volumes of the compartments were 1260 ml (background), 4.8 ml (left caudate), 4.9 ml (right caudate), 5.8 ml (left putamen), and 6.0 ml (right putamen). SNR was defined as the true value of structure activity concentration divided by the square root of the CRB. The SNR, Eq. (4), for detecting a 5% decrease in right putamen uptake, assuming 1.5 M detected counts, was 7.4 for USCB, 3.4 for FAN, and 3.2 for LEHR. The different volumes for each compartment gave rise to different SNR values in the LEHR data; this effect was amplified in the USCB data due to position dependent sensitivity.

Finally, we show in Fig. 9(a) reconstructed slices from the striatal phantom which demonstrate the improved performance of the USCB+FAN collimator pair, in comparison to FAN-only or LEHR only. The average precision measured over 20 Poisson noise realizations was 1.64% in the images of USCB+FAN collimation, which was better than that in the images of LEHR pair (2.89%) and FAN pair (2.38%). A

FIG. 8. SNR for striatal activity estimation for USCB and LEHR. The abscissa shows the total detected counts for the LEHR; USCB detected counts were higher for the same object activity distribution because of the increased sensitivity. Structure: background contrast was 5:1.

FIG. 9. (a) Transverse slice through reconstructed images of the striatal phantom with a 5:1 striatal/background concentration of ^{99m}Tc . (b) A profile through the putamen.

line profile through the middle of putamen was also obtained, Fig. 9(b).

4. CONCLUSIONS

We have confirmed that the novel collimator detected significantly more photons, especially those emitted near the focal axis. This experiment also revealed that the custom collimator contains some manufacturing variances; therefore, the measured system function, which reflects these variances, was incorporated into the reconstruction algorithm.

High-sensitivity brain SPECT imaging is expected to lead to improved performance in estimating striatal uptake. The novel collimator may be useful in early identification of Parkinson's disease, and in monitoring therapy response and disease progression.

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CONFLICT OF INTEREST DISCLOSURE

The authors have no COI to report.

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