Semiautomatic registration of 3D transabdominal ultrasound images for patient repositioning during postprostatectomy radiotherapy

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(Received 19 February 2014; revised 31 October 2014; accepted for publication 3 November 2014; published 2 December 2014)

Purpose: The aim of the present work is to propose and evaluate registration algorithms of three-dimensional (3D) transabdominal (TA) ultrasound (US) images to setup postprostatectomy patients during radiation therapy.

Methods: Three registration methods have been developed and evaluated to register a reference 3D-TA-US image acquired during the planning CT session and a 3D-TA-US image acquired before each treatment session. The first method (method A) uses only gray value information, whereas the second one (method B) uses only gradient information. The third one (method C) combines both sets of information. All methods restrict the comparison to a region of interest computed from the dilated reference positioning volume drawn on the reference image and use mutual information as a similarity measure. The considered geometric transformations are translations and have been optimized by using the adaptive stochastic gradient descent algorithm. Validation has been carried out using manual registration by three operators of the same set of image pairs as the algorithms. Sixty-two treatment US images of seven patients irradiated after a prostatectomy have been registered to their corresponding reference US image. The reference registration has been defined as the average of the manual registration values. Registration error has been calculated by subtracting the reference registration from the algorithm result. For each session, the method has been considered a failure if the registration error was above both the interoperator variability of the session and a global threshold of 3.0 mm.

Results: All proposed registration algorithms have no systematic bias. Method B leads to the best results with mean errors of −0.6, 0.7, and −0.2 mm in left–right (LR), superior–inferior (SI), and anterior–posterior (AP) directions, respectively. With this method, the standard deviations of the mean error are of 1.7, 2.4, and 2.6 mm in LR, SI, and AP directions, respectively. The latter are inferior to the interoperator registration variabilities which are of 2.5, 2.5, and 3.5 mm in LR, SI, and AP directions, respectively. Failures occur in 5%, 18%, and 10% of cases in LR, SI, and AP directions, respectively. 69% of the sessions have no failure.

Conclusions: Results of the best proposed registration algorithm of 3D-TA-US images for postprostatectomy treatment have no bias and are in the same variability range as manual registration. As the algorithm requires a short computation time, it could be used in clinical practice.
provided that a visual review is performed. © 2014 American Association of Physicists in Medicine. [http://dx.doi.org/10.1118/1.4901642]

Key words: postprostatectomy, radiotherapy, registration, ultrasound

1. INTRODUCTION

Prostatic bed radiation therapy (RT) is a common practice after radical prostatectomy for either adjuvant RT or salvage RT. The location of the prostatic bed can vary from session to session due to changes in the surrounding structures from rectal and bladder filling. Therefore, patient positioning based on the location of the prostatic bed before each radiation session is of major importance. The use of a three-dimensional (3D) transabdominal (TA) ultrasound (US) system could be a better alternative to x-ray-based modalities since US-based imaging offers better tissue contrast and is noninvasive and nonirradiating, avoiding the associated risks for the patient. Three different ultrasound image guided radiation therapy (IGRT) devices have been commercialized over the past 15 years, BAT® (Nomos, Pittsburgh, PA, USA), SonArray® (Varian, Palo Alto, CA, USA), and Clarity® (formerly named Restitu®) (Elekta, Stockholm, Sweden). Unlike the other systems, the latter uses an intra-modality approach based on the comparison of 3D-TA-US images acquired at each treatment session, to a reference 3D-TA-US image acquired during the planning CT acquisition. In clinical practice, a reference contour, drawn onto the reference US image, is manually translated on the daily US image in order to register the delineated structure and therefore retrieve the potential target displacement. For the prostatectomy localization, very few anatomical structures are visible on ultrasound unlike other treatment sites. Therefore, the recommended surrogate for prostatic bed positioning is the bladder neck which is defined by the bladder walls, except in the superior direction (Fig. 1). Several US/US registration algorithms, either intensity-based or feature-based, have been proposed in the literature and successfully applied to various sites such as breast, liver, kidney, heart, or prostate. However, to our knowledge, no automated approach has been investigated for the registration of 3D-TA-US/3D-TA-US postprostatectomy images. In this paper, the authors evaluate and compare quantitatively three different registration algorithms on a set of 62 3D-TA-US postprostatectomy images from seven patients.

2. MATERIAL AND METHODS

2.A. The US process for postprostatectomy repositioning

The US-IGRT system used to acquire the US images is the Clarity® device that has already been described elsewhere. It is based on a TA probe that uses a position sensor via optical tracking equipment (an infrared camera). For each acquisition, several hundred 2D-US slices are acquired during a probe sweep and are merged in a 3D image, based on their spatial location. The tracking system tracks the probe in its own coordinate system but refers to the room coordinate system defined by the room lasers thanks to a calibration. During the CT session, a reference 3D-TA-US image, denoted by USref, is acquired with the patient in the same position as for the CT acquisition. The CT image is already expressed in the room basis but the origin of CT coordinate system is not necessarily the lasers intersection, i.e., the simulation isocenter. The location of the simulation isocenter is determined by using radiopaque fiducial markers that are placed at the location of the patient skin marks and aligned with the room lasers. These markers can then be identified on the CT image. The USref and CT images are therefore both expressed in the room coordinate system and can be superimposed directly without the need of an additional registration as illustrated in Fig. 1.

During the planning phase, the clinical target volume (CTV) is delineated on the CT image. For postprostatectomy irradiation, it includes the bladder neck, the urethra-vesical anastomosis, the neurovascular bundles, the anastomosis, and the urethral axis as recommended by Poortmans et al. The Clarity workflow also requires an expert to manually delineate a reference positioning volume (RPV) on the USref image because organ volumes appear differently according to the used modality. Since US imaging allows for differentiation between soft tissues, enabling an accurate visualization of the bladder wall, the RPV contoured on the USref image is the bladder neck. To delineate this volume, the entire bladder is contoured on the USref image, then the volume is cropped superiorly leaving only the bladder neck (Fig. 1).

Over the treatment course, a daily 3D-TA-US image, denoted by USdaily, is acquired at the beginning of each treatment session fraction, and the patient is setup by registering the RPV onto the USdaily image. As there is currently no automatic registration algorithm available, the registration is entirely performed manually by trained radiation therapists. RPV is shifted only with translations to match the reference image.

Data from seven patients who underwent postprostatectomy RT and for which the US-IGRT system was used, have been retrospectively analyzed. In total, 62 USdaily images (5–15 images per patient) have been registered to their corresponding USref image.


As explained in Sec. 2.A, repositioning using the clarity system involves two steps. The first step is the manual segmentation of a RPV and the second step is the manual registration of the reference and daily images. To date, both steps are manual. The aim of this study is to propose an automatic method for the second step.

To do so, three methods based on mutual information (MI) have been tested. Indeed, MI is a widespread similarity
measure for monomodal and multimodal registration\textsuperscript{30} and has been used successfully to register ultrasound images.\textsuperscript{17,31}

The first method, denoted method A, directly applies MI on US\textsubscript{ref} and US\textsubscript{daily} images without any preprocessing. However, gray value information in US images may not be relevant in comparison with other modalities because of the presence of speckle noise and considering gradient information can improve the registration.\textsuperscript{32} Thus, the second method, denoted method B, computes MI between the gradient magnitude of the US\textsubscript{ref} and US\textsubscript{daily} images. The third method, denoted method C, combines gray value and gradient information. US\textsubscript{ref} and US\textsubscript{daily} images are preprocessed by calculating their importance images as proposed by Foroughi et al.\textsuperscript{13} and Kaar et al.\textsuperscript{25} The importance image is defined as a linear combination of the original gray level image, its gradient magnitude image and its Laplacian image. The relative weights between each component are chosen as suggested by Kaar et al.\textsuperscript{25} and are equal to 1/4, 1/2, and 1/4 for the gray level, gradient, and Laplacian images, respectively. One can notice that the methods A and B can be seen as a variation of the method C, the relative weights between each component being equal to 1, 0, 0 and 0, 1, 0 for the gray level, gradient, and Laplacian images, respectively.

The US\textsubscript{ref} and US\textsubscript{daily} images are considered as the fixed and moving images, respectively, as the RPV is defined on the US\textsubscript{ref} image. For each image, the foreground, i.e., the conic US field-of-view, is detected and used in the computation of the MI to consider only pairs of pixels that are in the conic US field-of-view of the two images. The registration is further limited to the tissues around the RPV to only consider the target volume displacement and to improve the algorithm robustness by restricting the registration to a region that has little anatomical variability. A region of interest (ROI) is defined on the fixed image as the intersection between the RPV volume dilated with a ball of radius \(r\) mm structuring element and the conic mask (Fig. 2).

The geometric transformation is limited to a 3D translation. The three parameters are optimized with the adaptive stochastic gradient descent algorithm.\textsuperscript{33} The MI is computed on sets of 5000 voxels stochastically selected from the ROI at each iteration. The stopping criteria of the optimization algorithm

\[ F \]
is the number of iterations fixed at 200. The whole process is performed using the elastix toolbox, which is based on the Insight Segmentation and Registration Toolkit (ITK).

2.C. Reference registration

Three trained operators have manually registered all 62 sessions using the Clarity® system. Registrations have been performed in a blind manner, the operators did not see the registrations of the others. The obtained translations are denoted \( T_{p,s,o} \) with \( p, s, \) and \( o \) being the patient, session, and operator indices, respectively. Shifts are expressed in terms of left–right (LR), anterior–posterior (AP), and superior–inferior (SI) directions. From these values, the interoperator variability IOV has been computed. Moreover, to see if the variability between the operators is more session specific or patient specific, the root mean square (RMS) of the misalignment vector lengths \( MV \) has also been calculated, \( \sqrt{\sum_{p=1}^{P} \sum_{s=1}^{S} T_{p,s,o}^2} / \sqrt{P \sum_{s=1}^{S} 1} \). The registered images are denoted \( r \) and \( s \) with \( r \) being the patient, session, and operator indices, respectively. These variabilities of variabilities are denoted intersession interoperator variability (ISIOV) and interpatient interoperator variability (IPIOV), respectively (Table I).

If the session standard deviation \( \sigma_{p,s} \) of the translations \( T_{p,s,o} \) between the three operators was above a threshold of 5 mm, the three operators were asked to redo their registrations. The obtained reviewed translations are denoted \( T'_{p,s,o} \) and have only been used to calculate a reference registration. The latter is defined as the average translation over the operators, \( \mu'_{p,s} = \frac{1}{3} \sum_{o=1}^{O} T'_{p,s,o} \). The IOV, ISIOV, and IPIOV are calculated with the original translation \( T_{p,s,o} \) values and not with the reviewed values.

2.D. Errors quantification

The three methods A, B, and C have been evaluated on the same dataset. The performance of the registration has been evaluated by calculating for each session the misalignment vector \( MV_{p,s} \) defined as the difference between the translation \( T_{p,s,o} \) found by the algorithm \( a \) and the reference registration \( \mu'_{p,s} \). The length of the misalignment vector \( LMV_{p,s} \) has also been calculated, \( LMV_{p,s} = ||T_{p,s,o} - \mu'_{p,s}||_2 \), where \( || \cdot ||_2 \) denotes the L2 norm. The weighted average of the misalignment vectors \( MV \) and the weighted average of the misalignment vector lengths \( LMV \) (\( MV = \frac{1}{P} \sum_{p=1}^{P} \sum_{s=1}^{S} MV_{p,s} \), \( LMV = \frac{1}{P} \sum_{p=1}^{P} \sum_{s=1}^{S} LMV_{p,s} \), where \( S_p \) denotes the number of session of the patient \( p \) and \( P \) denotes the total number of patient) have been calculated to get mean registration error values.

To quantify the accuracy and the precision of the algorithm session by session, the absolute error, i.e., \( |MV_{p,s}| \), and the error relative to the operator variability, i.e., \( |MV_{p,s}|/\sigma_{p,s} \), have jointly been considered to detect algorithm failures. For each session, the registration is considered as a failure if the absolute value of \( MV_{p,s} \) is both above a threshold of 3.0 mm, which is the order of magnitude of the IOV, and above the session standard deviation \( \sigma_{p,s} \) value. In these cases, the registration error is intrinsically small and inferior to the operator variability. The \( |MV_{p,s}| \) values in the first column of the histogram (\( i = 0 \)) are error values that can be intrinsically important but are still lower than the operator variability and therefore cannot be considered as failures since the reference value has a large variability. Likewise, the \( |MV_{p,s}| \) values in the first rows of the histogram (\( j < 3.0 \) mm) are small error values and cannot be considered as failures even if the error relative to the operator variability \( |MV_{p,s}|/\sigma_{p,s} \) is high. Indeed, in these cases, the three operators agree, i.e., \( \sigma_{p,s} \) approaches zero, and therefore \( |MV_{p,s}|/\sigma_{p,s} \) approaches infinity.

Table I. Interoperator, intersession, and interpatient variabilities.

<table>
<thead>
<tr>
<th>Variability</th>
<th>Abbreviation</th>
<th>Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interoperator</td>
<td>IOV</td>
<td>( \sqrt{\frac{1}{P} \sum_{p=1}^{P} \sum_{s=1}^{S} r_{p,s}} ) with ( r_{p,s} = \sqrt{\sum_{s=1}^{S} 1} )</td>
</tr>
<tr>
<td>Intersession</td>
<td>ISIOV</td>
<td>( \sqrt{\frac{1}{P} \sum_{p=1}^{P} \sum_{s=1}^{S} (\sigma_{p,s} - \mu_{p,s})^2} ) with ( \mu_{p,s} = \frac{1}{S_p} \sum_{s=1}^{S} \sigma_{p,s} )</td>
</tr>
<tr>
<td>Intipatient</td>
<td>IPIOV</td>
<td>( \sqrt{\frac{1}{P} \sum_{p=1}^{P} \sum_{s=1}^{S} (\sigma_{p,s} - \mu_{p,s})^2} ) with ( \mu_{p,s} = \frac{1}{S_p} \sum_{s=1}^{S} \sigma_{p,s} )</td>
</tr>
</tbody>
</table>

Note: \( P \) is the total number of patient \((P = 7 \text{ in this study}); S_p \) is the total number of session for the patient \( p \); RMS is the root mean square, \( \mu_{p,s} = \frac{1}{3} \sum_{o=1}^{O} T_{p,s,o} \), and \( \sigma_{p,s} = \sqrt{\frac{1}{3} \sum_{o=1}^{O} (T_{p,s,o} - \mu_{p,s})^2} \) are the mean and the standard deviation of the translations found by the three operators.

3. RESULTS

3.A. Manual reference registration

Table II shows the interoperator IOV, intersession ISIOV, and interpatient IPIOV variabilities in all directions. All variabilities are larger in AP direction and minimum in SI direction. Registration difficulties are more session-dependent than patient-dependent since ISIOV is larger than IPIOV for all directions.

3.B. Automatic registration results

Figure 3 shows the average of the misalignment vector lengths \( LMV \) as a function of the radius \( r \) for the methods A
Table II. Bladder-neck manual registration interoperator IOV, intersession ISIOV, and interpatient IPIOV variabilities in all directions. All values are in millimeters.

<table>
<thead>
<tr>
<th>Variability</th>
<th>LR</th>
<th>SI</th>
<th>AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOV</td>
<td>2.5</td>
<td>2.5</td>
<td>3.5</td>
</tr>
<tr>
<td>ISIOV</td>
<td>1.8</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>IPIOV</td>
<td>1.3</td>
<td>0.8</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Note: LR, left–right; SI, superior–inferior; AP, anterior–posterior.

Table III. Average misalignment vector $MV$ of the methods A, B, and C in all directions. All values are in millimeters.

<table>
<thead>
<tr>
<th>Method ($r$ value)</th>
<th>LR</th>
<th>SI</th>
<th>AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (20)</td>
<td>$-0.4 \pm 1.8$</td>
<td>$0.2 \pm 2.9$</td>
<td>$-0.3 \pm 2.3$</td>
</tr>
<tr>
<td>B (15)</td>
<td>$-0.6 \pm 1.7$</td>
<td>$0.7 \pm 2.4$</td>
<td>$-0.2 \pm 2.6$</td>
</tr>
<tr>
<td>C (15)</td>
<td>$-0.4 \pm 1.7$</td>
<td>$0.6 \pm 3.7$</td>
<td>$-0.5 \pm 2.4$</td>
</tr>
</tbody>
</table>

Note: LR, left–right; SI, superior–inferior; AP, anterior–posterior.

(dashed red line), B (solid green line), and C (dotted blue line). Method B is better than methods A and C. The optimal value of $r$ for method B is 15 mm but the error for neighbor values is only slightly larger. Table III shows the average misalignment vectors $MV$ of the methods A, B, and C calculated on all data using the best $r$ value for each method (20, 15, and 15 mm for method A, B, and C, respectively). No systematic bias has been noticed since $MV$ values are close to zero in every direction for all methods. In LR and AP directions, standard deviations are similar between each method as opposed to the SI direction for which method B has a lower standard deviation. Figure 4 shows the normalized joint histogram $h$ of the absolute value of the misalignment vector $|MV_{p,s}|$ and the absolute value of the misalignment vector normalized by the session interoperator variability $|MV_{p,s}|/\sigma_{p,s}$, for the method B in LR, SI, and AP directions, respectively. 95%, 82%, and 90% of the registration succeed for LR, SI, and AP directions, respectively. In 29% of the studied sessions, the algorithm fails in one direction and in 1.6% in two directions. It never fails in all three directions for the same session. The rate of sessions without failure is 69%.

4. DISCUSSION

The objective of this work was to propose and quantitatively evaluate registration algorithms of 3D-TA-US post-prostatectomy images in order to correct patient setup before RT treatment.

A first issue is registering 3D-TA-US images acquired by manual sweeping of the US probe on the abdominal wall, leading to different field-of-view between images. Moreover, the probe pressure induced by the manual acquisition can deform the tissues and is different between two acquisitions. Secondly, high anatomical variability could occur between sessions. Indeed, even with a strict protocol given to the patient,

![Fig. 3. Average of the misalignment vector lengths $LMV$ as a function of the radius of the ball structuring element used to dilate the RPV. The dashed (red), solid (green), and dotted (blue) lines show the $LMV$ of the methods A, B, and C, respectively. All values are in millimeters.

![Fig. 4. Normalized joint histogram for the method B of the absolute value of the misalignment vector $|MV_{p,s}|$ and the absolute value of the misalignment vector normalized by the session interoperator variability $\sigma_{p,s}$ in (a) left–right (b) superior–inferior, and (c) anterior–posterior directions. The horizontal and vertical lines (red lines) are the limits above which the registration fails. All values are in millimeters.](image-url)
it has been observed that the bladder filling varied from one session to the next. For these reasons, two preliminary steps are required before the registration: to compute a mask for the reference and the daily images and to define a ROI on the reference image to only consider the target volume displacement and to restrict the registration on a region that has little anatomical variability. The best size for the dilution of the RPVs is of 15 or 20 mm according to the considered method. Lower radii lead to degraded results because not enough image information around the structure of interest is included in the registration. Larger values, or using as ROI the entire conic US mask, lead to larger registration errors because the anatomical variabilities between the USref and USdaily images are too large. However, the $r$ value does not seem to be a very sensitive parameter since results are close for $r$ values in the range of 10–30 mm. Another difficulty related to the US modality is the presence of speckle noise in the images that differs from one image to the other. It could explain the better results found with method B that includes only gradient information, instead of the two others. On average (Table III), the variabilities of method B are smaller than the interoperator variabilities, which means that the level of precision of the proposed method is of the same order as the manual operators. The two other methods result in superior variabilities compared with the interoperator variability in the SI direction. On the other hand, the accuracy of the patient positioning is difficult to evaluate without a ground truth. Indeed, the reference used in this study is the average of the operators’ registrations that is not necessarily a perfect baseline.

Method C which includes gradient and gray value information has been proposed by Kaar et al. They compare various similarity measures to register 3D-TA-US images acquired on patients who received primary local radiotherapy for a prostate cancer. Using the mutual information by Mattes with the importance images, they find a $LMV$ value of $4.6\pm1.9$ mm to register intersession images. In the present study, the method C leads to a $LMV$ of $3.8\pm3.0$ mm. In addition to the difference of localizations (prostate vs prostatic bed), the reference registration of the two studies are different. Indeed, Kaar et al. use the ExacTrac system while in the present study the reference registration is calculated by averaging the manual registration values of three operators.

The use of the importance image (method C), which is a linear combination of the original gray level image, its gradient magnitude image and its Laplacian image, has been proposed by Kaar et al. Fifteen linear combinations of these three components have been tested,

$$II_{(w_1, w_2, w_3)} = w_1I + w_2\nabla I + w_3\Delta I$$

with

$$w_i \in \{0, 1/4, 1/2, 3/4, 1\} \forall i \in [1, 3], \sum_{i=1}^{3} w_i = 1,$$

where $II$, $I$, $\nabla I$, and $\Delta I$ are the importance image, the original image, the gradient image, and the Laplacian image, respectively, and $w_1$, $w_2$, and $w_3$ are the weights related to the images $I$, $\nabla I$, and $\Delta I$, respectively. The weights equal to $w_1 = 0$, $w_2 = 1$, and $w_3 = 0$ perform the best, which correspond to the method B.

Variations in bladder filling between sessions can affect the algorithm results. When the bladder filling is not sufficient, the contrast between structures such as the bladder neck is drastically degraded and can cause an algorithm failure. Figures 5(a) and 5(b) give an example of bladder filling variation between the reference and the daily 3D-TA-US images. On this pair of images, the algorithm B fails in one direction. This failure corresponds to the point of coordinates $(1.5, 6.5)$ in the LR joint histogram [Fig. 4(a)]. Another cause of failure is the lack of structures of interest in the daily US image. In some cases, the US probe sweep acquisition performed by the radiation therapist is not large enough to capture the entire bladder neck leading to truncating of the bladder neck. Figure 5(d) gives an example of a truncated volume in comparison to the reference image [Fig. 5(c)]. On this pair of images, the algorithm B fails in two directions. This failure corresponds to the points of coordinates $(1.5, 4.5)$ and $(1.5, 7.5)$ in the SI and AP joint histograms, respectively [Figs. 4(b) and 4(c)]. In such cases, a rescanning would have been appropriate.

One limitation of the present study is the absence of quantification of the rotations. As mentioned by Klayton et al. and Zhu et al., the prostate bed rotational motion is patient specific but can be quite important in some cases. However, neither the clinical software, which allows only manual translations, nor the treatment couch used in our department is able to take such movements into account. Therefore, rotations cannot be compared to a reference for validation or used to correct patient misalignment. An interesting approach would be to take them into account to improve both the image registration and the patient setup. Likewise, the proposed methodology still needs an expert to manually contour the RPVs during the planning process. An interesting prospect would be to automate this step in order to have a fully automatic method rather than a

![Fig. 5](image-url)
semathematical one. Automatic segmentation, which is in gen-
eral a difficult task, has never been investigated on US images
in case of prostatectomy patients. One difficulty is linked to the
definition of the bladder neck which is ambiguous because it is
not an anatomical organ. In contrast, the CTV, which is always
manually delineated on the planning CT image for postprost-
tectomy radiotherapy, even if there is no image guidance, could
also be used for registration since the CT image and the refer-
ce US image are in the same coordinate system (Fig. 1). Us-
ing such a ROI instead of the RV would probably not change
draastically the results since the two volumes encompass almost
the same area. However, the results would have been more
difficult to compare to the current clinical registration since the
latter is done manually by translating the RV.

Finally, it should be noted that the computation time needed
to perform a registration is about 40 s on a single core Intel
Xeon CPU E31225 @ 3.10 GHz without any particular optimi-
zation. As the algorithm requires a short computation time, it
could be used in clinical practice without needing an additional
time.

5. CONCLUSION

The proposed semiautomatic registration algorithm based
only on gradient information is a reliable approach to setup pa-
tients irradiated after a prostatectomy using a US-based IGRT
modality. The results of this algorithm have no bias and are in
the same variability range as manual registration. As the algo-
rithm requires a short computation time, it could be used in
clinical practice provided that a visual review is performed.

ACKNOWLEDGMENTS

This work is supported in part by the Lyric Grant No. INCa-
DGOS-4664 and is within the framework of the LABEX
PRIMES (ANR-11-LABX-0063) of Université de Lyon,
within the program “Investissements d’Avenir” (ANR-11-
IDEX-0007) operated by the French National Research Agency
(ANR). The authors specially want to thank all radiation ther-
apists who helped them with this study.

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