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Citation for published version (APA):

Sammali, F., Blank, C., Xu, L., Huang, Y., Kuijsters, N. P. M., & Schoot, B. C. (2018). Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking. *Biomedical Physics & Engineering Express*, 4(3), [035012]. <https://doi.org/10.1088/2057-1976/aab053>

DOI:

[10.1088/2057-1976/aab053](https://doi.org/10.1088/2057-1976/aab053)

Document status and date:

Published: 13/03/2018

Document Version:

Accepted manuscript including changes made at the peer-review stage

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
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- The final published version features the final layout of the paper including the volume, issue and page numbers.

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Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

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Abstract. Recent research suggests uterine contractions to play an important role for the success of conception. Unfortunately, the lack of tools for quantitative analysis limits our understanding of the uterine contractility outside pregnancy. More recently, several methods based on speckle tracking have gained attention for assessment of uterine contractility; however, the absence of a ground truth hampers the optimization of any tracking method. To overcome this limitation, here we present an experimental setup based on a human *ex-vivo* uterus able to generate controlled uterine motion with the aim of assessing the accuracy of motion tracking techniques and obtaining clear indications on the optimal imaging setting. Uterine motion was obtained by use of an electromagnetic actuator generating a controlled, sinusoidal displacement of a syringe piston, injecting 3-mL saline water through a balloon catheter inserted into the uterine cavity. This way, controlled, rhythmic uterine motion was generated while maintaining the original speckle characteristics. The use of the proposed setup was tested for comparison of ultrasound speckle tracking methods. Block-matching by sum of absolute differences (SAD) with three different block sizes was employed as a use case for speckle tracking evaluation. Correlation coefficient (r), mean square error (MSE), and Hausdorff distance (H_d), were the adopted objective metrics for evaluating the speckle tracking performance. Two needle markers inserted in the uterus, along with the driving signal of the actuator, represented the reference for assessing the speckle tracking accuracy. SAD was optimized and compared for its agreement with the reference signals. The results show the tracking performance of SAD with larger block size ($1.724 \times 1.724 \text{ mm}^2$) to produce the most accurate tracking ($p < 0.05$). To conclude, the realized proposed experimental setup represents a realistic ground truth for uterine motion, allowing objective evaluation of speckle tracking techniques and aiding with the choice of the optimal imaging settings for quantitative imaging of uterine motion outside pregnancy.

Keywords: Experimental setup, Speckle tracking, Motion analysis, Uterine motion, Block matching, Uterus.

Submitted to: *J. Phys. A: Math. Gen.*

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

1. Introduction

Ultrasound (US) imaging represents a valid, non-invasive, and safe option for quantitative analysis of the uterus and can be used as an alternative to invasive techniques, such as intrauterine pressure measurements, and hysterosalpingoscintigraphy, in order to investigate the uterine mechanical function (Birnholtz 1984). Current knowledge on uterine motion is however limited. Only qualitative evaluation of uterine motion has been performed, evidencing variations of uterine contractile patterns during the menstrual cycle (Bulletti et al. 2000) and the important role of peristaltic movements on infertility treatment outcome (IJland et al. 1999). Accurate interpretation of the resulting US image sequences is challenging also for skilled and experienced operators (Bulletti & de Ziegler 2006). Therefore, the operator-dependency of qualitative ultrasound analysis hampers its adoption for assessment of the uterine function in relation to uterine dysfunctions and infertility. Motion tracking by US imaging is an active field of scientific research that has already been translated into several applications; in particular, for cardiovascular (Lopata et al. 2010) and muscular (Kawagishi 2008) investigations. A general approach, not requiring access to the US scanner hardware and radio frequency (RF) signals, consists of tracking the characteristic speckle pattern of ultrasound gray-level images (Wagner et al. 1986), (Burckhardt 1978).

The characterization of the uterine motion outside pregnancy, and in relation to uterine dysfunctions, is not trivial due to several technical and clinical challenges, such as complex and irregular patterns, complex multilayer uterine structure and speckle distribution, limited and slow uterine motion as compared to neighboring structures, and speckle anisotropy and depth dependency. Against these challenging aspects, a speckle tracking algorithm can be designed and optimized for quantification of uterine motion. Quantitative analysis by use of motion tracking and strain imaging has so far only been performed either *in-vitro*, by the use of dedicated phantoms producing fluid-driven motion (Hobson et al. 2008) or *ex-vivo*, by applying a freehand palpation to an *ex-vivo* uterus to produce mechanical stimulus for US strain imaging (Hobson et al. 2007). However, assessing the quality of the developed methods is challenging due to the lack of a reliable reference for the uterine strain and motion.

In this paper, we propose a system for objective evaluation of the speckle tracking performance on an *ex-vivo* uterus, whose controlled rhythmic motion is generated by a dedicated experimental setup. The resulting speckle pattern reproduces that of a real uterus. The *ex-vivo* uterus was marked with two hypodermic needles to produce clear markers. Objective metrics were employed for speckle tracking evaluation. As a use case to evaluate the utilization of the proposed experimental setup, this was tested to optimize the block size for speckle tracking by block-matching with sum-of-absolute differences (SAD) cost function. The results confirmed that the realized experimental setup can support the development of uterine motion and strain imaging methods by providing objective comparison/evaluation of the tracking performance.

2. Method

2.1. Experimental setup

The realized setup permits generating a controlled, sinusoidal, and linear displacement of a syringe piston for inducing uterine rhythmic motion. Figure 1 shows an overview of the experimental setup.

Figure 1. The experimental setup.

2.1.1. Hardware Uterine motion is generated by an electromagnetic actuator. The adopted electromagnetic actuator is a servo motor (SMH4OS, Kinco, Shenzhen, China) generating rotary motion at its output shaft, as shown in Figure 1. The voltage driving the actuator is generated by a National Instrument (NI) Board (USB 6341, National Instruments, Austin, Tx, USA), which is connected to a laptop and controlled by dedicated software implemented in LabView® (National Instruments, Austin, TX, USA). The driver (IndraDrive HCS02, Bosch Rexroth, Boxtel, The Netherlands), which works in analog voltage mode, receives the driving voltage to control the motor. A screw-slider system with pitch equal to 1.8 mm is connected to the output shaft of the motor in order to convert rotary motion into linear motion at the slider. The motor and the slider are mounted on a metal frame, as shown in Figure 1. A syringe is employed for fluid injection into a balloon catheter, which is placed into the uterine cavity of the *ex-vivo* uterus. The barrel of the syringe is fixed to a holder mounted on the metal frame of the screw-slider system, while the plunger of the syringe is connected to the slider such that its motion is facilitated. By moving the slider forward and backward, the plunger of the syringe can slide injecting and withdrawing fluid through the balloon catheter, respectively. This way, repetitive inflation and deflation of the *ex-vivo* uterus is generated, thus simulating the rhythmic uterine motion. The angular position of the motor shaft is monitored by a rotary encoder embedded in the motor, providing feedback for accurate plunger positioning.

2.1.2. Software LabView® software is employed to implement the actuator control as well as to realize the system user interface. A sinusoidal motion (injection volume)

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking⁴

is adopted to mimic real uterine motion, choosing a period equal to one cycle of the simulated rhythmic uterine motion, as shown in Figure 2a. The injection volume is then converted into motion range of the syringe plunger based on the diameter of the adopted syringe. The adopted motion results in a sinusoidal velocity of the plunger as shown in Figure 2b. The velocity of the plunger is then converted into rotary velocity of the motor, according to the pitch of the screw equal to 1.8 mm.

Figure 2. Velocity of the syringe (a) and injection volume (b) during inflation and deflation of the *ex-vivo* uterus for mimicking peristaltic uterine movement.

The injection volume, the inflation and deflation time (period in seconds), and the initial position of the syringe can be independently adjusted by the operator.

The core software is implemented in a while loop using a feedback control scheme. Inside each loop, the real time position of the syringe plunger is first measured by the rotary encoder. A state machine is then adopted to determine the next state of the actuator, i.e., inflating, deflating, or no motion, based on the current state and the measured position of the plunger. The instantaneous velocity is first determined according to the next state and position of the plunger and then sent to the NI Board controlling the motor driver. The execution time of one loop is about 10.1 ms, resulting in a sampling frequency of the position /rotary encoder of 90 Hz. The entire program flow chart is shown in Figure 3.

2.1.3. Measurement protocol for validation US acquisition was performed at the Catharina Hospital Eindhoven (the Netherlands). The surgery for uterus removal was preventive laparoscopic hysterectomy (LH); therefore, the removed uterus presented benign pathology. The patient signed an informed consent prior to the surgery, and

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

Figure 3. Flow chart of the control software implemented in LabView®.

all acquired post-surgical imaging was exempt from Regional Ethics Review Board approval, under the legal requirements for clinical research in the Netherlands. 4-min US recording was performed in saline water on the *ex-vivo* uterus, immediately after LH. An US scanner WS80A (Samsung) equipped with a trans-vaginal V5-9 probe imaging at 5.6-MHz (central frequency) was employed for the US acquisition. The acquisition frame rate was 30 frames/s, which was amply sufficient to meet Nyquist condition given the limited bandwidth of uterine motion (Bulletti et al. 2000). The acquired gray-level data were then exported in AVI (Audio Video Interleave) format for off-line analysis, implemented in Matlab® (MathWorks, Natick, USA). This implied the use of log-compressed data, as implemented in all US scanners for visualization purpose. Immediately after LH, the human *ex-vivo* uterus was first marked with two hypodermic needles (MagellanTM, Mansfield, USA, 0.813 mm diameter, 3.8 cm length), as shown in Figure 4, to realize clear markers as a reference for uterine motion tracking. The *ex-vivo* uterus was then submerged in a saline water-filled plastic container, and sustained by a polyvinyl chloride (PVC) transparent foil fixed at the two sides of the container. A sterile syringe was employed to inject 3-mL of saline water through a balloon catheter

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

Figure 4. *Ex-vivo* uterus marked with two hypodermic needles.

(Codan pvb medical GmbH, Lensahn, Germany). In order to avoid air bubbles into the uterine cavity, the balloon catheter was inserted into the uterine cavity under saline water, and sutured, similar to a drain (Hornbrey et al. 2000), with a surgical knot tied tightly above the cervix of the *ex-vivo* uterus. Motion artifacts were avoided by holding the trans-vaginal probe with a US probe holder during the acquisition. An acoustic absorber was positioned on the bottom of the container for limiting US reflection and reverberation while imaging the *ex-vivo* uterus.

Rhythmic uterine motion was induced with periodic (sinusoidal) inflation and deflation of the uterine cavity. A period of 20 s (0.05 Hz), corresponding to an average uterine contraction period (Bulletti et al. 2000), was set to generate one cycle of the rhythmic uterine motion. Finally, we operated the experimental setup with synchronized US B-mode recording.

This way, realistic and controlled uterine motion was generated while maintaining the original speckle characteristics of the uterus. Figure 5 shows the complete setup (experimental setup and *ex-vivo* uterus).

Figure 5. The complete setup (experimental setup and *ex-vivo* uterus) inducing simulated rhythmic uterine motion for validation of speckle tracking algorithm.

2.2. Speckle tracking evaluation strategy

Evaluation and optimization of 2D speckle tracking by block matching was performed on the human *ex-vivo* uterus by means of the proposed experimental setup. For each

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

US loop acquired, twelve blocks were positioned around each marker (needles) with a distance equal to twice the speckle size (typical block size) as well as in a way that shadowing from the needles was avoided (Fig. 6).

Figure 6. Trans-vaginal ultrasound image of the *ex-vivo* uterus. Example of blocks' position in the first frame (a) and in the subsequent frame (b) before and after volume injection in the uterine cavity, respectively. The two white circles indicate the center of the blocks placed on top of the two hypodermic needles (marker 1 and 2) while the two orange circles indicate the center of two of the twelve surrounding blocks, here provided as an example. The two markers are tracked over time by optical flow while the two surrounding blocks are tracked over time by block-matching.

The markers were automatically tracked over time by optical flow (OF) based on Lucas-Kanade algorithm with a neighborhood size (number of equations) experimentally chosen equal to twice the speckle size ($1.724 \times 1.724 \text{ mm}^2$); this method was proven to be especially suitable for needle tracking (Lee et al. 2008). The 12 surrounding blocks were simultaneously tracked over time by the 2D speckle tracking method under evaluation. The markers, together with the sinusoidal driving signal of the electromagnetic actuator, represent the reference for assessing the speckle tracking accuracy.

In order to validate the experimental setup motion, the two markers were first compared with the driving signal. Then, to assess the performance of the 2D speckle tracking algorithm for its ability to follow the (reference) motion of the two markers, the estimated motion of the surrounding blocks was compared with the motion of their respective markers.

2.3. Objective measures for speckle-tracking evaluation

Correlation coefficient (r) and mean square error (MSE) are standard similarity measures that can be used to evaluate the agreement between the absolute motion of the reference signals, as well as between the motion of the two markers and their surrounding blocks. Here, Hausdorff distance (H_d) (Huttenlocher et al. 1993) is also adopted as an additional distance metric to evaluate the similarity between the trajectories followed by the blocks and reference signals. H_d is here used as a boundary point matching between

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

the reference signals (reference trajectories) and the estimated motion of the blocks (estimated trajectories).

In general, given two trajectories of points $A = a_1, \dots, a_i$ and $B = b_1, \dots, b_j$, H_d can be expressed as

$$H(A, B) = \max(\vec{h}(A, B), \vec{h}(B, A)), \quad (1)$$

with

$$\vec{h}(A, B) = \max_{a \in A}(\min_{b \in B} \|a - b\|) \quad (2)$$

being the directed Hausdorff distance from A to B. The Euclidean distance between each point a_i on trajectory A and all points b_j on trajectory B is first calculated and then the minimum is chosen. This process is repeated for all points a_i on trajectory A and the maximum distance for trajectory A with respect to trajectory B is found. The distance $\vec{h}(A, B)$ is not symmetric, therefore, between the two directions, $\vec{h}(A, B)$ and $\vec{h}(B, A)$, the maximum is considered.

H_d is a measure of the spatial distance between two trajectories of points and it represents the maximum deviation between two compared trajectories. H_d is a representative index not only of the distance of contours in absolute terms, but also of the shape of a trajectory of points.

Similarity analysis was performed between the absolute motion of the two moving markers and the one of their surrounding blocks. This way, twenty-four values (twelve for the comparison between marker 1 and its surrounding blocks, and twelve for the comparison between marker 2 and its surrounding blocks) per each similarity measure were obtained. Mean and standard deviation of the 24 r , MSE, and H_d values were then calculated.

2.4. Use case of speckle tracking-evaluation

Uterine motion was quantified by employing 2D speckle tracking based on a sum-of-absolute differences (SAD) cost function for block-matching. Prior to speckle tracking, each image in the acquired loops was first preprocessed to regularize the spatial resolution, here represented by the speckle size. The convexity of the adopted transvaginal probe enhances the anisotropy and depth dependency of the image resolution, complicating the block-matching implementation. Therefore, image regularization was obtained by Wiener deconvolution filtering after performing an *in-vitro* experiment as proposed in (Kuenen et al. 2013). After regularization, the resulting images presented an isotropic resolution with speckle size of 0.862 mm, calculated as the full-width half-maximum of the autocorrelation function (Wagner et al. 1983).

Being the adopted frame rate (30 Hz) relatively high compared to the slow myometrial movement ≤ 2 mm/s (IJland et al. 1997), the US images were up-sampled in space (bilinear interpolation) by a factor of 2 to increase the tracking resolution and to detect sub-pixel motion.

Off-line analysis of the collected gray-level data consisted of performing a block-matching

algorithm based on SAD to track the controlled uterine speckle movement. For a block-matching design, two critical parameters must be determined: block size and search area. The block size should represent the lower limit, determined by the speckle size (now isotropic and constant over the US image), to find a unique match in the following frame. Larger blocks reduce the chance of finding spurious matches but limit the spatial resolution of the uterine displacement estimates. The search area should be as small as possible to minimize the computational complexity, yet covering the maximum expected displacement of the block in case of maximum uterine tissue velocity. In order to determine the search area needed for block matching analysis, each search area was adjusted to cover the maximum displacement expected between two consecutive frames. The controlled uterine speckle motion estimation was performed across subsequent frames with three different block sizes. In particular, $0.431 \times 0.431 \text{ mm}^2$ (*BSize1*), $0.862 \times 0.862 \text{ mm}^2$ (*BSize2*), and $1.724 \times 1.724 \text{ mm}^2$ (*BSize3*) block sizes were used that correspond to half, once, and twice the speckle size, respectively.

2.5. Statistical analysis

According to Shapiro-Wilk test (Shapiro & Wilk 1965), all data were not Gaussian distributed ($p < 0.05$). Therefore, the three adopted block sizes were compared per each adopted similarity measure, r , MSE, and H_d , by Kruskal-Wallis test (Breslow 1970) for establishing the significance level (p value) of the mean values. Wilcoxon signed rank test (Woolson 2008) was then performed as multi-comparison test between the three groups. For all the analyzes, the confidence level α was set at 0.05.

3. Results

Figure 7 shows an example of trajectory for the reference signals provided by marker 1 and by the voltage driving the actuator.

Figure 8 shows an example of trajectory for marker 1 compared with the trajectory of the estimated uterine motion by tracking a surrounding block with SAD using *BSize3*. Table 1 reports the similarity results when comparing the reference signals, markers and driving signal, for validation of the experimental setup motion.

Table 1. Similarity results. Comparison between the trajectories of the driving signal of the piston and the two markers.

Ref Signals	r	MSE	H_d
Marker1 - DrSig	0,974	0,008	0,406
Marker2 - DrSig	0,958	0,019	0,041

The values of the adopted similarity measures for assessment of SAD tracking are plotted in Figure 9 in terms of mean $\pm$ standard deviation. The values are obtained for the three

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

Figure 7. Example of comparison between the trajectory of the driving signal of the piston and marker 1 during 4 cycles. In the graph, the blue signal represents the driving signal. The two signals are normalized and aligned in time.

Figure 8. Example of comparison between the trajectory of marker 1 and one of its surrounding blocks (a). Example of comparison between the trajectory of marker 2 and one of its surrounding blocks (b). The two trajectories in both (a) and (b) start from the same position and they refer to the blocks' placement depicted in Figure 6. Here, the surrounding blocks are tracked by SAD with $BSize3$ (twice the speckle size).

adopted block sizes ($BSize1$, $BSize2$ and $BSize3$) when comparing the markers with their surrounding blocks. These results are obtained averaging the 24 values obtained from the similarity analysis between markers and surrounding blocks for each block size. Our statistical analysis on the MSE results reveal the separation between the three different groups ($BSize1$ - $BSize2$, $BSize1$ - $BSize3$, and $BSize2$ - $BSize3$) to be significant ($p < 0.05$), with $BSize3$ showing the best performance.

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

Figure 9. Similarity results: a) Correlation coefficient results for SAD cost function with the three adopted block sizes (*BSize1*, *BSize2* and *BSize3*). The results are reported in terms of mean $\pm$ standard deviation; b) MSE results for SAD cost function with the three adopted block sizes (*BSize1*, *BSize2* and *BSize3*). The results are reported in terms of mean $\pm$ standard deviation. The asterisk (*) indicates a significant difference ($p < 0.05$); c) H_d results for SAD cost function with the three adopted block sizes (*BSize1*, *BSize2* and *BSize3*). The results are reported in terms of mean $\pm$ standard deviation.

4. Discussion

Motion and strain analysis by US speckle tracking has recently gained attention for the assessment of the uterine motion. However, the optimization of this technology is hampered by the lack of a ground truth. The proposed experimental setup based on a human *ex-vivo* uterus is proven useful for the evaluation of US speckle tracking providing a realistic ground truth for uterine strain imaging and motion analysis. The high agreement reported in Table 1 and obtained by comparing our reference signals, i.e., the two markers and driving signals, shows the ability of the two markers to follow the well controlled uterine motion induced by our experimental setup. This result confirms the validity of the proposed setup to generate controlled rhythmic motion of an *ex-vivo* uterus. The obtained agreement allowed us to consider OF tracking of the two needle markers as a reference for assessing the quality of block-matching algorithms for their ability to follow the (controlled) motion of these markers. For the tested SAD block matching algorithm with different block sizes, significant difference ($p < 0.05$) was revealed by the performed Kruskal-Wallis test only when MSE was employed as a similarity measure. Based on Wilcoxon signed rank test, the performance of SAD tracking with the three adopted block sizes was significantly different, revealing SAD tracking with *BSize3* ($1.724 \times 1.724 \text{ mm}^2$) to produce the best performance. Also when a significant difference was not found, our results showed that SAD tracking improved its performance with increased block size at the expense of worse spatial resolution (Friemel et al. 1995). A possible explanation may be that SAD metrics are affected by time variations of the signal mean and variance; a larger block contains more samples and those variations are mitigated by the included larger statistics (Bohs & Trahey 1991), (Trahey et al. 1987).

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

We only tested block sizes up to twice the speckle size because larger block sizes would be too large compared to the myometrium size and the resulting spatial resolution would hamper the analysis.

The developed experimental setup leads to motion limitations compared to real uterine peristalsis (UP). UP is known as rhythmic wave-like motion that propagates along the myometrium in different directions for different phases of the natural menstrual cycle (Kuijsters et al. 2017). Our setup is not able to generate a propagating wave that mimics such a real condition. However, reproducing real UP goes beyond the objective of this study, which focuses on generating controlled tissue motion maintaining the original uterine speckle characteristics for objective evaluation of speckle tracking performance. The elastic properties (compliance) of uterine tissue may result in local dephasing of the motion pattern, possibly affecting our similarity analysis. Compliance and deformation also cause decorrelation between subsequent frames. However, this effect is typically neglected for distances within a matching block. As the distance between neighboring blocks was kept on the order of the block size, we can assume local deformation and dephasing to be negligible for the considered short distances.

In this study, our experimental setup was used for evaluation of speckle tracking techniques with B-mode imaging data; however, performance evaluation on radio-frequency (RF) data is also possible. Moreover, unhealthy uteri with pathologies such as adenomyosis, endometriosis or leiomyoma could be employed. Pathological uteri may be characterized by different speckle and the tissue motion may differ with respect to healthy uterine tissue; therefore, by marking with needles both the pathological and healthy tissue, it would be possible to assess differences in tissue strain. This way, we could understand the influence of pathological uteri on uterine motion enabling doctors and physicians to enrich their diagnostic information and improve treatment.

5. Conclusion

An experimental setup based on a human *ex-vivo* uterus is proposed for evaluation of US speckle tracking techniques aimed at quantitative analysis of uterine motion. This experimental setup generates controlled uterine tissue motion while maintaining the original uterine speckle characteristics, thus providing a realistic ground truth for objective evaluation of US speckle tracking techniques. The recorded US videos can therefore support with the choice of optimal imaging settings for uterine motion and strain quantification in clinical studies. To this end, many other speckle tracking algorithms, such as normalized cross-correlation, mean square differences, and non-normalized correlation, can be tested and compared beyond SAD, employing different block sizes.

Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking

Acknowledgements

We acknowledge the Dutch STW HTSM-13901 grant, which includes a financial contribution from the companies Ferring and Samsung.
We acknowledge the help of Cristina Caresio from the "Politecnico di Torino", Italy, with the measurements in the hospital.

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*Experimental setup for objective evaluation of uterine motion analysis by ultrasound speckle tracking*14

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