Peer Review File

Article information: https://dx.doi.org/10.21037/atm-21-5049

First External Peer Review

Reviewer A

This paper presents a clinical study comparing 3D US and computer guided punctures to conventional approaches.

The paper would be improved a lot if following the recommandations:

- first of all, the state of the art is not appropriate: the cited references correspond to research aspects (needle detection, steering, etc.) which are not totally relevant whilst nothing is said about existing products providing more or less the same service - I mean US 2D or 3D and EM tracking (from Brainlab, Koelis, Philips, and certainly many others) .

Revision:

Thank you for your suggestion.

We have included some new studies and references at your request.

Part of introduction

At present, there are software-based and hardware-based methods for enhanced positioning and the ability to track the needle in a 3D ultrasound volume. Hardware methods currently include the use of piezoelectric actuators to vibrate the needle, the use of 3D power Doppler ultrasound to segment the vibrating bending needle, and the placement of a small ultrasonic sensor on the surgical tool to detect the sound waves transmitted during the 3D ultrasound imaging process by moving the needle pen and detect the induced intensity change of ultrasonic volume to detect the needle in the 3D ultrasonic volume and other methods.[7-10] The existing software-based methods cover the use of principle component analysis (PCA) to detect the 3D ultrasound volume needle, and the use of radar transformation based on the radio frequency (RF) signal obtained by the 3D ultrasound probe to locate the needle.[11-12] Real-time algorithms to track the linear surgical instrument under the 3D ultrasound volume, using Parallel Integral Projection (PIP) transformation to locate the thin needle inserted into the 3D ultrasound image.[13-15] The advantages of 3D imaging are well established in a variety of clinical settings. Albrecht H et al. studied the feasibility of real-time 3D ultrasound guided biopsies and found that 3D ultrasound guided biopsies can be performed using multi-plane views or a combination of cross sections and rendered images. In distinguishing malignant from benign lesions, 3D ultrasound-guided biopsies produced 35 true positive results, 12 true negative results, and 5 false negative results. The sensitivity and specificity of diagnosis of malignant tumor were 87.5% and 94.4%, respectively. [16] An Chao et al. compared the feasibility and efficiency of the 3D visual ablation planning system (3DVAPS) assisted by ultrasonic-guided percutaneous microwave ablation (US-PMWA) with the conventional two-dimensional hepatocellular carcinoma (HCC) plan (diameter > 3 cm). The median follow-up was 21 months. Compared with the 2D planning group, the number of inserts, ablation time, ablation energy, and the success rate of the first ablation were higher in the 3D planning group, [17] indicating that 3DVAPS improved the accuracy of US-guided ablation, resulting in reduced LTP and 5 mm-AM HCC lesions with a diameter greater than 3 cm. More recently, 4D ultrasound can be used to generate patient-specific models in preparation for intervention. And 4D ultrasound can be used for real-time motion tracking, which is useful for local ablation.[18]

- some elements are not defined: what is a success? how is it assessed ? what is the size of targets?

Revision:

Thank you for your suggestion.We added this in Methods.

Definition of operation success and failure

For puncture surgery (percutaneous vascular puncture, percutaneous puncture biopsy, percutaneous bile duct puncture), it is a success that the needle accurately reaches the target location and obtains the doctor's desired sample. If the location is not reached or the sample is not obtained, it is a failure. For nerve block surgery (thoracic paravertebral nerve block, sciatic nerve block), the accurate arrival of the needle to the target location and the injection of certain drugs are considered successful, if the location is not reached or the injection of drugs is considered a failure.

Some other details:

- line 150, you write "an accurate sensor": how accurate is it? please explain how the accuracy has been tested. Are there any artefacts due to metallic objects around?

Revision:

Thank you for your suggestion.It is not convenient for us to disclose the design process in this article, but we have cited relevant literature to prove the advanced nature of our design.

Discussion

Novel 3D B-ultrasound imedis9000 has the characteristics of comfortable screen display, accurate sensor, flexible mechanical arm, dust-free design, and wide compatibility of ultrasonic interface (Figure 12). First of all, its screen display is compatible with ultrasound grayscale and suitable surgical brightness, which is in line with the doctor's surgical vision habits. The theoretical value of the sensor can reach 0.5mm; the accuracy can reach 1.5mm. Zhao Yue et al has reported that the tip localization error in his study was within 1.5mm and the axis accuracy was within 1.6mm,which was consistent with our design.[11]

- line 195 and 221, you mention "puncture time and puncture times"; this is confusing. For the second one you should use "number of trials"

Revision:

Thank you for your suggestion.

We have followed your advice and change them into "number of trials" .

There are also many repetitions in the discussion.

Revision:

Thank you for your suggestion.

We rewrote the discussion section and moved the results section to the discussion section based on other reviewers' comments.

Regarding literature, work from SINTEF in Norway from Lango or Reinerstein and colleaguesshould be cited aside from commercial products. It would be much more relevant than the references 2 to 8 (at least).

Revision:

Thank you for your suggestion.

We have included some new studies and references at your request.

Part of introduction

At present, there are software-based and hardware-based methods for enhanced positioning and the ability to track the needle in a 3D ultrasound volume. Hardware methods currently include the use of piezoelectric actuators to vibrate the needle, the use of 3D power Doppler ultrasound to segment the vibrating bending needle, and the placement of a small ultrasonic sensor on the surgical tool to detect the sound waves transmitted during the 3D ultrasound imaging process by moving the needle pen and detect the induced intensity change of ultrasonic volume to detect the needle in the 3D ultrasonic volume and other methods.[7-10] The existing software-based methods cover the use of principle component analysis (PCA) to detect the 3D ultrasound volume needle, and the use of radar transformation based on the radio frequency (RF) signal obtained by the 3D ultrasound probe to locate the needle.[11-12] Real-time algorithms to track the linear surgical instrument under the 3D ultrasound volume, using Parallel Integral Projection (PIP) transformation to locate the thin needle inserted into the 3D ultrasound image.[13-15] The advantages of 3D imaging are well established in a variety of clinical settings. Albrecht H et al. studied the feasibility of real-time 3D ultrasound guided biopsies and found that 3D ultrasound guided biopsies can be performed using multi-plane views or a combination of cross sections and rendered images. In distinguishing malignant from benign lesions, 3D ultrasound-guided biopsies produced 35 true positive results, 12 true negative results, and 5 false negative results. The sensitivity and specificity of diagnosis of malignant tumor were 87.5% and 94.4%, respectively. [16] An Chao et al. compared the feasibility and efficiency of the 3D visual ablation planning system (3DVAPS) assisted by ultrasonic-guided percutaneous microwave ablation (US-PMWA) with the conventional two-dimensional hepatocellular carcinoma (HCC) plan (diameter > 3 cm). The median follow-up was 21 months. Compared with the 2D planning group, the number of inserts, ablation time, ablation energy, and the success rate of the first ablation were higher in the 3D planning group, [17] indicating that 3DVAPS improved the accuracy of US-guided ablation, resulting in reduced LTP and 5 mm-AM HCC lesions with a diameter greater than 3 cm. More recently, 4D ultrasound can be used to generate patient-specific models in preparation for intervention. And 4D ultrasound can be used for real-time motion tracking, which is useful for local ablation.[18]

Reviewer B

Reference needed at line 49 to justify that precise needle positioning and tracking to improves intervention success and reduces the incidence of adverse complications

Revision:

Thank you for your suggestion.

We have followed your advice.

Introduction

Some diagnostic and therapeutic clinical procedures (such as biopsies, therapeutic injections, nerve blocks, and anesthesia) involve needle intervention. These procedures require precise needle positioning and tracking to improve intervention success and reduce the incidence of adverse complications.[1-2] Ultrasound imaging is a low-cost, real-time, noninvasive imaging method that is widely used to guide needle insertion interventions. However, imaging the target anatomy using traditional two-dimensional (2D) ultrasound is often challenging because of the need to perfectly align the ultrasound probe in order to include the needle in the imaging plane. In addition, using 2D ultrasound requires an accurate interpretation of the patient's 3D anatomy based on a series of 2D ultrasound images, which often depends on the physician's level of experience.[3-4]

An alternative approach refers to employ 3D ultrasound to guide needle insertion.[5] In fact, 3D ultrasound, providing volumetric imaging data, can visualize both the needle and the 3D anatomical structures without the need to perfectly align the ultrasound probe. However, the visibility of the needle in 3D ultrasound volumes might be degraded by several factors (e.g., ultrasound speckle that reduces the quality of ultrasound data, the bright linear structures in the ultrasound volume that have appearance close to the needle, as well as the reflection of the ultrasound beam by the needle in a direction away from the ultrasound probe). [6] To address the mentioned limitations, automatic needle localization and tracking methods have been developed to detect the needle in 3D ultrasound volumes.

Reference needed at line 53 to justify that physician experience is a relevant factor

Revision:

Thank you for your suggestion.

We have followed your advice.

Introduction

Some diagnostic and therapeutic clinical procedures (such as biopsies, therapeutic injections, nerve blocks, and anesthesia) involve needle intervention. These procedures require precise needle positioning and tracking to improve intervention success and reduce the incidence of adverse complications.[1-2] Ultrasound imaging is a low-cost, real-time, noninvasive imaging method that is widely used to guide needle insertion interventions. However, imaging the target anatomy using traditional two-dimensional (2D) ultrasound is often challenging because of the need to perfectly align the ultrasound probe in order to include the needle in the imaging plane. In addition, using 2D ultrasound requires an accurate interpretation of the patient's 3D anatomy based on a series of 2D ultrasound images, which often depends on the physician's level of experience.[3-4]

An alternative approach refers to employ 3D ultrasound to guide needle insertion.[5] In fact, 3D ultrasound, providing volumetric imaging data, can visualize both the needle and the 3D anatomical structures without the need to perfectly align the ultrasound probe. However, the visibility of the needle in 3D ultrasound volumes might be degraded by several factors (e.g., ultrasound speckle that reduces the quality of ultrasound data, the bright linear structures in the ultrasound volume that have appearance close to the needle, as well as the reflection of the ultrasound beam by the needle in a direction away from the ultrasound probe). [6] To address the mentioned limitations, automatic needle localization and tracking methods have been developed to detect the needle in 3D ultrasound volumes.

Reference needed at line 68 for PCA- and RF-based approaches

Revision:

Thank you for your suggestion.

We have followed your advice.

Introduction

At present, there are software-based and hardware-based methods for enhanced positioning and the ability to track the needle in a 3D ultrasound volume. Hardware methods currently include the use of piezoelectric actuators to vibrate the needle, the use of 3D power Doppler ultrasound to segment the vibrating bending needle, and the placement of a small ultrasonic sensor on the surgical tool to detect the sound waves transmitted during the 3D ultrasound imaging process by moving the needle pen and detect the induced intensity change of ultrasonic volume to detect the needle in the 3D ultrasonic volume and other methods.[7-10] The existing software-based methods cover the use of principle component analysis (PCA) to detect the 3D ultrasound volume needle, and the use of radar transformation based on the radio frequency (RF) signal obtained by the 3D ultrasound probe to locate the needle.[11-12] Real-time algorithms to track the linear surgical instrument under the 3D ultrasound volume, using Parallel Integral Projection (PIP) transformation to locate the thin needle inserted into the 3D ultrasound image.[13-15] The advantages of 3D imaging are well established in a variety of clinical settings. Albrecht H et al. studied the feasibility of real-time 3D ultrasound guided biopsies and found that 3D ultrasound guided biopsies can be performed using multi-plane views or a combination of cross sections and rendered images. In distinguishing malignant from benign lesions, 3D ultrasound-guided biopsies produced 35 true positive results, 12 true negative results, and 5 false negative results. The sensitivity and specificity of diagnosis of malignant tumor were 87.5% and 94.4%, respectively. [16] An Chao et al. compared the feasibility and efficiency of the 3D visual ablation planning system (3DVAPS) assisted by ultrasonic-guided percutaneous microwave ablation (US-PMWA) with the conventional two-dimensional hepatocellular carcinoma (HCC) plan (diameter > 3 cm). The median follow-up was 21 months. Compared with the 2D planning group, the number of inserts, ablation time, ablation energy, and the success rate of the first ablation were higher in the 3D planning group, [17] indicating that 3DVAPS improved the accuracy of US-guided ablation, resulting in reduced LTP and 5 mm-AM HCC lesions with a diameter greater than 3 cm. More recently, 4D ultrasound can be used to generate patient-specific models in preparation for intervention. And 4D ultrasound can be used for real-time motion tracking, which is useful for local ablation.[18]

Before line 72, please explain what is meant by "the electromagnetic navigation real-time positioning and ultrasonic image of the 3D multi-mode intelligent intervention" How is EM navigation used? What matters the system intelligent? 73 system (novel 3D B-ultrasound imedis9000)was applied

Revision:

Thank you for your suggestion.

We fully answered the question in our discussion.We also included the results in the discussion and the original discussion in the introduction according to your request.

Sentence at lines 83-84 unclear. What is meant by "Cutaneous vascular puncture, percutaneous biopsy, percutaneous bile duct puncture, thoracic paravertebral nerve block, sciatic nerve block operations were performed, respectively"? With respect to what? Please make this clearer to better reflect Figure 1

Revision:

Thank you for your suggestion.

We have added some explanation

Study design and setting

The present prospective, double-center, randomized study was conducted on cases recruited from the Affiliated Hospital of Nantong University and Nanjing First Hospital , Nanjing Medical University. This study included 190 cases who needed puncture, from 2 centers, and were randomly divided into a control group (conventional 2D B-ultrasound instrument, n=95) and an experimental group (novel 3D B-ultrasound imedis9000, n=95). Percutaneous vascular puncture, percutaneous needle biopsy, percutaneous bile duct puncture, thoracic paravertebral nerve block, and sciatic nerve block were performed, respectively.To be more specific, in the control group, percutaneous vascular puncture(n=12), percutaneous needle biopsy(n=35), percutaneous bile duct puncture(n=16), thoracic paravertebral nerve block(n=13), and sciatic nerve block(n=17) and in the experimental group, percutaneous vascular puncture(n=12), percutaneous needle biopsy(n=34), percutaneous bile duct puncture(n=16), thoracic paravertebral nerve block(n=13), and sciatic nerve block(n=18). The specific experimental design and the number of cases in each group are shown in Figure 1.

At lines 131-132 please specify how the sample sizes were determined. How did you use SPSS software to compute sample size?

Revision:

Thank you for your suggestion.

I'm really sorry, this is a clerical error, we are using Graphpad Prism 8.0 software, we have modified.

Statistical analysis

We carried out the analyses largely based on Graphpad Prism 8.0, and p-value < 0.05 was reported with statistics-related significance. We compared continuous information based on an individual *t*-experiment in the two groups.

Lines 150 - 187 should be removed. In the methods it is stated that "The advantages and disadvantages of the two puncture methods were prospectively analyzed in cases, and the feasibility of electromagnetic navigation real-time positioning and ultrasonic image 3D multi-modal intelligent intervention system was assessed" Therefore the results should reflect this alone. Opinions regarding the characteristics and advantages of the system are irrelevant

Revision:

Thank you for your suggestion.We included the results in the discussion and the original discussion in the introduction according to your request.

Discussion

Novel 3D B-ultrasound imedis9000 has the characteristics of comfortable screen display, accurate sensor, flexible mechanical arm, dust-free design, and wide compatibility of ultrasonic interface (Figure 12). First of all, its screen display is compatible with ultrasound grayscale and suitable surgical brightness, which is in line with the doctor's surgical vision habits. The theoretical value of the sensor can reach 0.5mm; the accuracy can reach 1.5mm. Zhao Yue et al has reported that the tip localization error in his study was within 1.5mm and the axis accuracy was within 1.6mm,which was consistent with our design.[11] The mechanical arm of 3D multi-modal intelligent intervention ultrasound can be regulated in multiple degrees of freedom. In addition, the instrument can be sterilized directly and has excellent dust-proof performance. Its ultrasound interface is compatible with mainstream ultrasound. 3D multi-modal intelligent intervention ultrasound can combine electromagnetic navigation real-time positioning with ultrasound images to provide an efficient, intelligent and concise interactive interface, which is termed as 3D multi-modal intelligent hybrid. As a result, the clinical puncture path and angle can be designed prior to the operation, and the puncture angle is no longer as limited as the conventional method. During the operation, the operator can monitor the puncture path and needle tip position in real time, which greatly elevates the success rate of the operation. In addition, if the target point of the puncture is shifted during the operation, the device can promptly give an intelligent reminder. Furthermore, when the puncture reaches the target point of the lesion, the device will also give an intelligent reminder.

We have synchronously matched the coaxial positioning channel puncture needle (Figure 13), which has three characteristics. Firstly, the coating absorbs super slippery coating technology, which has less resistance, and most cases feel painless under most conditions. Secondly, the material is imported stainless steel material, which has good toughness, strength and resistance. Corrosion performance, biocompatibility and consistency can better meet the needs of interventional systems. Thirdly, a number of series and specifications of disposable access trocars have been designed and manufactured, covering biopsy puncture, anesthesia puncture, radiofrequency and microwave therapy, spinal foraminal puncture and other occasions, and mainstream interventional therapy consumables are used with precision. The mentioned coaxial positioning channel puncture needles provide great convenience for the puncture process.

Compared with the conventional 2D ultrasound instrument, the novel 3D B-ultrasound imedis9000 has obvious advantages in many applications. The novel 3D B-ultrasound imedis9000 has a small footprint, high flexibility, and does not require complex setup and preoperative preparation. It supports a variety of surgeries (e.g., spinal and spinal space-occupying, nerve compression and spinal degenerative variations). Because it does not rely on large imaging instrument, it can show its magic in minimally invasive day surgery on the spine. In addition, the novel 3D B-ultrasound imedis9000 combines ultrasonic and magnetic navigation with an accuracy of 1.5mm, which does not rely on ultrasound for spatial identification of puncture instruments, effectively avoiding the volume effect of conventional ultrasound and making depth positioning more accurate. Preoperative puncture angle design is no longer limited, puncture path and needle tip position are monitored in real time during operation, intraoperative intelligent reminder of lesion target deviation and intraoperative intelligent reminder of lesion target arrival, clear puncture path planning and intuitive real-time stereotactic positioning (Figure 14) . The novel 3D B-ultrasound imedis9000 is simple in navigation setup, and can dynamically stack multiple surgical paths during surgery to meet the needs of surgery. Moreover, it combined with magnetic navigation avoids large amounts of radiation and protects medical personnel. Compared with conventional ultrasound, the operation is simple, greatly reducing the learning time, and reducing the difficulty of puncture and surgery.

In the present study, the puncture time and number of trials of the experimental group using the novel 3D B-ultrasound imedis9000 were significantly lower than those of the control. No significant difference was identified in basic vital signs between the two groups before and after surgery. The success rate of the novel 3D B-ultrasound imedis9000 was 100%, and the success rate of the conventional 2D B-ultrasound instrument was 95.7%. It is noteworthy that one of the biggest advantages of novel 3D B-ultrasound imedis9000 is that it can accurately perform nerve block. The peripheral nerve is a complex highly heterogeneous structure with variable micro anatomical architecture from root to terminal branch. Ultrasound, a nerve localization technique, permits a detailed and person-specific examination of the anatomy covered in peripheral nerve block. Medical US exploits sound waves in the frequency range of 3-15 MHz. Nerve visualization requires the use of probes with the capability of producing US at 10-15 MHz. Ultrasound at the mentioned frequencies presents prominent spatial resolution, allowing the discrimination of nerve architecture. The ultrasonographic appearance of nerves varies with anatomical location and the quantity of connective tissue within the nerve.[19] A description of the challenges in image interpretation and common image-related anomalies has been published.[20-21] However, our technical positioning is more precise, and the operation is more convenient. The most interesting thing is that we have designed and manufactured multiple series and specifications of disposable access trocars, covering biopsy puncture, anesthesia puncture, radiofrequency and microwave therapy, spinal foraminal puncture, etc., and the precise use of consumables significantly mitigates the suffering of cases.

Indeed, this study had certain limitations. First, our research centers are relatively small, with only 2 research centers, and we look forward to including more research centers in the future. Second, the types of operations should increase, and novel 3D B-ultrasound instruments were employed (e.g., microwave ablation). Third, more cases should be surveyed for satisfaction and follow-up of postoperative complications.

Lines 206 - 216 should be removed from the discussion or at least moved into the Introduction

Revision:

Thank you for your suggestion.We included the results in the discussion and the original discussion in the introduction according to your request.

Second External Peer Review

Reviewer A

This randomised, double-centre study compares the use of 3D B-ultrasound with electromagnetic (EM) navigation and conventional 2D B-ultrasound to guide needles in puncture procedures. This patient study highlights the benefits of using the former approach in terms of puncture time, number of trials and success rate. However, the manuscript is a bit messy (some text is repeated and some text should be moved to other sections), does not provide enough context of this study, does not highlight the novelty of their research, does not give enough details of the study protocol, and describes just the characteristics of the 3D B-ultrasound system so the study seems biased to using this system. More details as follows:

- In Introduction, regarding the context of the study, the authors do not detail the use of electromagnetic tracking systems to track the needle in 3D ultrasound (the approach used in their study, the title mentions multi-modal intelligent intervention system due to using EM tracking) although other software-based and hardware-based methods are described. The limitations of those approaches and why EM tracking could be an interesting approach are not presented. Previous literature comparing 3D ultrasound and 2D ultrasound for microwave ablation guiding biopsies and guiding biopsies (patient studies) was presented but the authors do not highlight the novelty of their study.

Revision:

Thank you for your suggestion.

We have changed this in the introduction and added some introduction about EM.

See line 82-90.

We included an extra paragraph on our invention to prove the novelty of the research.

See line 99-127.

- In Methods, the authors detailed aspects of the study such as the puncture procedure, how many patients per group and treatment, ethics approval, inclusion/exclusion criteria, unblinded study, variables to be measured, statistical analysis and trial registration. However, they do not describe the protocol used for guiding the needle in the case of 3D B-ultrasound with EM navigation (for example, which type of visualization was used [orthogonal views, rendered images…]) either in the case of 2D B-ultrasound. In the former, some specifications of the setup would be appreciated: for instance, what the working volume of the EM tracking system is, where the EM field generator was placed related to the patient, whether the puncture path and angle were designed prior to the operation, how the needle was tracked (specifically, where the EM sensor was attached to the needle) and if the doctor tried to follow the puncture path and angle designed previously with the tracked needle. On the other hand, which 2D ultrasound station/stations were used and their characteristics should be also mentioned.

Revision:

Thank you for your suggestion.

We have marked different parts of the instrument in Figure 1, and we have described the instrument in the experimental method.For puncture needles, we have added Table 1 to show the types and specifications.

See line 99-127.

We also added the 2D ultrasound instrument (Siemens, Germany).

See line 155.

- In Clinical trial results, the authors present the findings but they also interpret the results (this should be in discussion). Examples are sentences like “which indicates that there is no obvious personal bias”, “suggesting that the two surgical methods had no significant effect on cases’ vital signs” and “the adoption of the novel 3D B-ultrasound imadis9000 can clearly define puncture path planning, intuitive real-time stereoscopic positioning, greatly improve the success rate of puncture and shorten the operation time”. In Figure 2 and Figure 5, the legend might be wrong. It represents preoperative blood indicators and preoperative prothrombin time (figure 2) and absolute value of vital sign change (figure 5) for both groups but the legend specifies before and after surgery where it should be control group and experimental group. If the legend is not wrong, then the statistical analysis based on t-test would not be valid because there would be two factors: group and time. On the other hand, Figures 6-11 show images of each type of puncture procedure for the 3D ultrasound station. Do they represent the puncture path planning performed prior to the operation?

Revision:

Thank you for your suggestion.

We have placed some of the results in the discussion section according to your request.

See line 234-261.

The illustrations and images of Figures 2 and 5 have been changed, as well as the content of the presentation.

See new Figure 5 and Figure 7.

Figure 9-14 represents the puncture path planning performed prior to the operation.

- In Discussion, the authors mentioned “the theoretical value of the sensor can reach 0.5 mm; the accuracy can reach 1.5 mm”. What is the “value of the sensor”? Is it the precision? On the other hand, the authors describe characteristics of the 3D B-ultrasound imedis9000 and the coaxial positioning channel puncture needle that should be moved to Methods. Why and how do they authors have synchronously matched the coaxial positioning channel puncture needle? The authors should also describe why they have designed and produced a number of series and specifications of disposable channel trocars.

Revision:

Thank you for your suggestion.

In order not to cause ambiguity, we delete the theoretical value of the sensor. We have moved the needle part to the method part. Based on the different needle types and specifications required by different surgeries, we set up a variety of needle types to facilitate the use of more convenient(Table 1).

See line 99-127.

Other recommendations:

- Use the same terms throughout the text. For example, "ultrasound-guided" biopsies, "ultrasound guided" biopsies and "US-guided" ablation.

Revision:

Thank you for your suggestion. All terms have been modified to the same expression.

- Check the use of respectively (line 36, line 97…): https://www.springer.com/gp/authors-editors/authorandreviewertutorials/writinginenglish/use-of-respectively/10252704).

Revision:

Thank you for your suggestion. We have used the correct words.

- Add a space after colon and after comma (line 26, line 39...). Remove space before comma (line 94, line 260...).

Revision:

Thank you for your suggestion. We have modified the way we use punctuation.

- In Study design and setting, remove the text related to the number of patients per group and puncture procedure (lines 97-100) since it is described in Figure 1.

Revision:

Thank you for your suggestion. The content has been removed .

- The puncture procedures, the number of centres and the number of patients are repeated several times (for example, in Study design and setting, in sample size and in Clinical trial results). Maybe you can remove some text and combine some sections to avoid it.

Revision:

Thank you for your suggestion. We have reduced the number of times that phrase appears.

- Replace future tense with past tense in Ethical Statement, Ethics approval and informed consent, Exclusion criteria, Adverse events, Monitoring and quality assurance and Patient involvement.

Revision:

Thank you for your suggestion. All tenses have been modified correctly.

- In Interventions, specify the anaesthesia of percutaneous vascular puncture and percutaneous bile duct puncture.

Revision:

Thank you for your suggestion. We have added this. All biopsies and nerve blocks were carried out with local anesthesia (lidocaine 1%).

See line 157.

- Check the text in Patient involvement. It is related to the researchers instead of the patients.

Revision:

Thank you for your suggestion. We have modified it correctly.

- Specify company of 3D B-ultrasound imedis 9000 and of the 2D B-ultrasound station/stations.

Revision:

Thank you for your suggestion.

We have added this.

- Line 34: percutaneous instead of cutaneous.

Revision:

Thank you for your suggestion. We have modified it correctly.

- Line 88: 95 instead of 180.

Revision:

Thank you for your suggestion.We have modified it correctly.

- Line 87: 2D B-ultrasound instead of 2B-ultrasound.

Revision:

Thank you for your suggestion. We have modified it correctly.

- Line 257: are instead of were.

Revision:

Thank you for your suggestion. We have modified it correctly.

- Line 273: "We declare that we…" instead of "we declare that they…".

Revision:

Thank you for your suggestion. We have modified it correctly.

- Define 3D (line 54), LTP, AM (line 81) and 4D (line 81).

Revision:

Thank you for your suggestion.

We have added this.

- Figure 1: Include blood routine indicators and prothrombin time in flow chart. Extend curly bracket to include all puncture procedures.

Revision:

Thank you for your suggestion.

We have changed this.

- Figure 2 and Figure 5: include units and meaning of "ns".

Revision:

Thank you for your suggestion.

We have added this.

- Figure 3 and Figure 4: include meaning of "***".

Revision:

Thank you for your suggestion.

We have added this.

- Figure 6 to Figure 10: remove the text that describes type of puncture procedure above the image since this information is also in the figure caption. What do the green (or maybe grey) line represent?

Revision:

Thank you for your suggestion.

We have followed your suggestions. We have added :The red line in each picture represents the puncture path, and the green cross represents the final part of the puncture.

- Figure 9: What do the colours inside the green box represent? Is it a doppler US image?

Revision:

Thank you for your suggestion. We have added :The green box on the right represents the electromagnetic signal.

- Figure 12 to Figure 14: remove the information that is already described in other parts of the manuscript.

Revision:

Thank you for your suggestion. We have followed your suggestions.

- On Figure 12, indicate where the EM field generator is.

Revision:

Thank you for your suggestion.

We have added this in figure 1.

Reviewer B

Below is my peer-review report:

• General: The article concentrates on using a 3D multi-modal intelligent intervention system to navigate during several types of surgical biopsies and injections in the group of 95 patients with the control group of 95 patients.

• Specific:

1) Abstract

Correct

Revision:

Thank you for your suggestion. We have revised into a new one and this way of writing also has the requirements of the magazine itself.

Abstract:

Background: Anesthesia, nerve block, therapeutic injections, and biopsies all require an acupuncture intervention. However, traditional two-dimensional (2D) ultrasound-guided needle puncture is often challenging and therefore requires the use of three-dimensional (3D) ultrasound images to accurately identify and evaluate the patient's anatomical structure.

Methods: In this study, a 3D multi-modal intelligent intervention system using electromagnetic navigation for real-time positioning and ultrasound images was described. A total of 190 cases requiring puncture were randomly divided into control (conventional 2D ultrasound instrument) and experimental (novel 3D ultrasound imedis9000) groups. The advantages and disadvantages of the two puncture methods were prospectively analyzed in the 190 cases, and the feasibility of electromagnetic navigation real-time positioning was compared to ultrasound imaging.

Results: This study included 190 cases from two centers that required puncture treatment and were randomly assigned to the control (conventional 2D ultrasound instrument; n = 95) or the experimental (novel 3D ultrasound imedis9000; n = 95) groups. Percutaneous vascular puncture, percutaneous biopsy, percutaneous bile duct puncture, thoracic paravertebral nerve block, and sciatic nerve block operations were performed separately. The results indicated that the puncture time and number of trials in the experimental group were significantly lower than those in the control group. No significant difference was identified in the basic vital signs between the two groups before and after surgery. The success rate of the novel 3D ultrasound imedis9000 was 100%, and the success rate of the conventional 2D ultrasound instrument was 95.7%. Furthermore, the results also showed that the novel 3D ultrasound imedis9000 and the matching coaxial positioning channel puncture needle had low pain, good toughness and strength, and great convenience.

Discussion: The new 3D multi-modal intelligent intervention system using electromagnetic navigation real-time positioning and ultrasound images has significant advantages compared with conventional 2D ultrasound in terms of puncture time,

number of trials, operation difficulty, and convenience, and is worthy of further promotion and use in clinics.

See line 26-44.

2) Introduction

Would you please give more information about the physicians who performed the procedures (number, experience)?

Revision:

Thank you for your suggestion.

We have added this: Three experienced chief physicians participated in each operation.

See line 157.

3) Exclusion criteria

III-please give more detailed information-did any medical scales disqualify patients from the intervention?

Revision:

Thank you for your suggestion.

I'm really sorry that there is no scale evaluation for this part when designing the project. We will pay attention to this in the future design scheme.

4) Would you please give more details about the 2D B-ultrasound machine?

Revision:

Thank you for your suggestion.

We have added this: The control used conventional 2D ultrasound instrument (Siemens, Germany).

See line 155.

5) Clinical trial results

Would you please explain why to analyze the preoperative blood routine indicators and differences in basic vital signs between these two groups of patients? Do they have any impact on the choice of the medical procedure? Would it not be more enjoyable for the readers to explain the difficulties and possible complications of the methods used?

Revision:

Thank you for your suggestion.

We made a little mistake earlier, and we've corrected it.

We analyzed the preoperative blood routine indicators and prothrombin time of the 190 cases enrolled in experiment and control group, and found no significant difference between the two groups, which indicates that there is no obvious personal bias in this study. No significant difference was identified in basic vital signs between the two groups before and after surgery, suggesting that the two surgical methods had no significant effect on cases' vital signs. The puncture time and number of trials of the experimental group were significantly lower than those of the control. The success rate of the novel 3D ultrasound imedis9000 was 100%, and the success rate of the conventional 2D ultrasound instrument was 95.7%. Our study confirms the feasibility, convenience and safety of the novel 3D ultrasound imedis9000.

See line 211-221.

6) Discussion

There are mentioned lots of advantages of 3D B-ultrasound which were not analyzed in the study (e.g. simple operation, reduced learning time, difficulty of puncture). Would you please make the discussion more compatible with the issues examined in the study?

Revision:

Thank you for your suggestion.

we put this section in the lab materials section so it's easier to read.

7) References

Correct

Revision:

Thank you for your suggestion.

We have corrected this.

8) Figures

Please include a legend with descriptions of all symbols used in each figure.

Revision:

Thank you for your suggestion.

We have corrected this.

Please include higher quality pictures with more precise legends, arrows and symbols.

Revision:

Thank you for your suggestion.

We have corrected this.

The discussion is not very compatible with the analyzed material. There are needed more accurate data to compare groups between them. The quality of photos from ultrasound and their interpretation should be better.

Revision:

Thank you for your suggestion.

We have corrected this.

See line 224-276.

Reviewer C

Line 31: correct to " real-time positioning was compared to ultrasonic image"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 33: change 2 to "two" (This includes any other mention of numerical value, must be written out).

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 35: change to " nerve block and sciatic nerve"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 36: change " as revealed ..." to " Results indicate that puncture"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 39: change from " In addition" to " Furthermore, we"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 49: remove '"( )"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 57: replace "An alternative approach refers to employ" to "Newer approaches such as the, 3D ultrasound"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 58: change to " imaging data which visualized both the needle.."

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 64: change "At present" to "Currently"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 74 and 78: include source # from references

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 86: add space ") was applied".

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 122: add space after the comma

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 138: change occurring to "that occurred"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 139: change will then report to "reported"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 151: Replace "For puncture surgery (percutaneous vascular puncture, percutaneous puncture biopsy, percutaneous bile duct puncture), it is a success" with " During the puncturing portion of the surgery, this included percutaneous vascular puncture, percutaneous puncture biopsy, percutaneous bile duct puncture. This was considered a success if the needle accurately reaches the target location and obtains the doctor's desired sample."

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 177-180: Remove sentence, it is too repetitive. Instead can write. " Based on out ur study design, we also analyzed the preoperative blood routine indicators..."

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 186: space after '(figure 5), ..."

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 194: change has the characteristics of " to "provides"

Revision:

Thank you for your suggestion. We have modified it correctly.

Line 195: Change the beginning of the sentence to, " Advantages include..."

Revision:

Thank you for your suggestion. We have modified it correctly.

Reviewer D

The subject sounds interesting but abstract alone has a vast number of grammatical errors and the title makes no clear sense. The paper appears to be automatically translated. I would recommend the paper be sent back for basic copy editing prior to re-submission for review of its scientific merit.