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Template for MR visualization and needle targeting

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Abstract

To improve the targeting accuracy and reduce procedure time in MRI-guided procedures, a 3D-printed flexible template was developed. The template was printed using flexible photopolymer resin FLFLGR02 in Form 2 printer® (Formlabs Inc, Somerville, MA). The flexible material gives the template a unique advantage by allowing it to make close contact with human skin and provide accurate insertion with the help of the newly developed OncoNav software. At the back of the template, there is a grid comprised of circular containers filled with contrast agent. At the front of the template, the guide holes between the containers provide space and angular flexibility for needle insertion. MRI scans are initially used to identify tumor position as well as the template location. The OncoNav software then pre-selects a best guide hole for targeting a specific lesion and suggests insertion depth for the physician. A phantom study of 13 insertions in a CT scanner was carried out for assessing needle placement accuracy. The mean total distance (TD) error between planned and actual insertion is 2.7 mm, the maximum error was 4.78 mm and standard deviation was 1.1 mm. The accuracy of the OncoNav-assisted and template-guided needle targeting is comparable to the robot-assisted procedure. The proposed template is a lowcost, quickly-deployable and disposable medical device. The presented technology will be further evaluated in prostate cancer patients to quantify its accuracy in needle biopsy.

Keywords

MRI-guided procedure; 3D-printed template; MRI-visible; OncoNav

3. Introduction

Prostate cancer is common site of malignancy in men²⁰. Approximately 1 million prostate biopsy procedures are conducted in the US each year^{4,17} for the diagnosis of prostate cancer. Image-guided biopsy is able to increase the accuracy of prostate cancer diagnosis by providing physicians image-based feedback during the biopsy procedure. Transrectal Ultrasound (TRUS) and Magnetic Resonance Imaging (MRI) have been commonly used as

the modalities for prostate imaging and image-guided biopsy. TRUS is widely available for guiding prostate biopsy but prostate tumors often are not visible in ultrasound. MRI, especially multi-parametric MRI is currently the most promising imaging modality for detecting prostate cancer with great accuracy^{10,30}. MRI-TRUS fusion for guidance of targeted prostate biopsy has been reported in the literature^{27,31,41}. However, prostate patients without rectum are excluded from this method and ultrasound artifacts oftentimes compromise the efficiency of the image fusion^{6,32}. An early investigation by D'Amico A.V., et al, performed transperineal MRI-guided prostate biopsy in an open configuration 0.5 Tesla MRI scanner¹¹. Since then, the advancement of prostate MRI imaging and interventional devices as well the availability of wide bore MRI scanners favorable for interventional use have enabled in-bore biopsies to be performed more easily^{2,9,19,21,38}. Robotics are understood to be an effective method to overcome the problem of limited patient access inside the bore of MRI scanner. Also, the high accuracy of the robotic procedure has been widely recognized. Fichtinger et al. firstly reported designs of a manually powered platform for prostate interventions in a closed MR system^{1,5,14,15}. Since then, development of prostate robots has been demonstrated in closed MRI scanners^{12,13,22,35}. However, the addition of a robotic operation onto the current interventional procedure requires a significantly modified clinical workflow and extensive training. Moreover, certain parts of the robots have a negative impact on the Signal-to-Noise(SNR) in the MR image.

Alternatively, some studies have investigated the possibility of improving template biopsies without disrupting clinical workflow. Given the fact that the diagnostic outcome from this freehand approach is strongly dependent on the physician's skills and experience, repetitive biopsy insertions and sampling are very common, which increases the potential risks and complications of the procedure. Beekley Medical (Bristol, CT) has developed a fiducial marker (PinPoint®) that can improve the accuracy of freehand needle insertion⁴. But the marker provides the surgeon with limited positional guidance. The other effective approach is to use a template or grid and provide the relative positional information of the tumor to the physicians. So far, most of the templates available in the market or reported in the research can only achieve a 2-dimensional vertical insertion and have been mainly used in Ultrasound and CT modalities. Table 1–2 shows the current development of CT/MRI compatible assistive needle guidance system. Kokoda J., et al, has reported using a specially designed needle guidance template to perform the prostate biopsy in a 70cm bore 3T MRI³⁷. The promising result shows an improved accuracy compared to conventional freehand procedure. However, the conventional MRI marker-based registration is used, which requires the physician to manually enter the positions of the MRI markers of the Z-frame read from the scanner console.

In this paper, an innovative 3D-printed template has been developed and manufactured which combines the advantages of both a fiducial marker and template, to improve the real-time biopsy procedure. First, the template is flexible, which means it can follow the contour of the patient and lies on the skin allowing the physician to carry out freehand needle insertion without any additional training. Second, it provides MRI-visibility in both coronal and transverse planes on MRI. Third, the software OncoNav allows the template to fast-register with the pre-operative MRI image and provides predicted needle trajectory, which will reduce the procedural time to a great extent without disruption to the current clinical

flow. A phantom study has been done inside a CT scanner to test accuracy. Finally, it is low cost and disposable because it is 3Dprinted from commonly available resin as raw material. In the future, it will be tested in clinical trials to prove its effectiveness and accuracy.

4. Materials and Methods

The final printed version of the template will be directly mounted on the patient's body. There will be a guidance system for the physician to insert the needle at different angles and hit the tumors at different locations. (Figure 1)

4.1. Design Criteria

Our design criteria are based on a survey of interventional radiologists who frequently perform prostate interventions. The general criteria show the features which a template should have to meet the market demand, environmental regulations, training and setup requirement, site restrictions, patient accessibility and safety. The operational criteria show the technical requirement for the template such as the dimension, method of insertion, MRI visibility and contact surface (Table 3).

4.2 Flexible Template Design

The template was initially designed in Solidworks® (Solidworks Corporation, Waltham, MA). The template should be large enough to cover the whole perineal region. The size of the template is 80mm×80mm, which is finalized after consultation with physician in NIH lab facilities. It has 144 Gadolinium (Gd) containers (Figure 2 (a)), each container is filled with diluted Gd solution for MRI visualization. The material used for printing out the template is flexible photopolymer FLFLGR02 manufactured by Formlabs® (Formlabs Inc, Somerville, MA). The advantage of using the 3D printing method over other fabrication method is its low cost and fast-prototyping. The template is designed for 16, 17 and 18 G biopsy or treatment needles, which are commonly used needle sizes for clinical trials in NIH facilities.

The print was tested on a platform with maximum curvature of 120 degree. The cap for closing the Gd containers is designed to have one insertion module. The circular shaped module underneath is for closing the Gd container. In addition, double-sided tape was used to firmly attach the template onto the patient body during the operation. The mechanical design of the template has experienced systematic optimizations. The idea is to make a template that is both durable and easy-to-use. Figure 3 illustrates the detailed design consideration.

4.3 Image Contrast

There are two factors that should be taken into consideration in order to make sure the template can be MRI visible under any circumstances. One is container size, the other is the concentration of the Gd solution. These two factors are independent to each other. The MRI scans were conducted to find out the suitable diameter for optimal MRI signal intensity.

4.4 Preparation of contrast agent

To find out the optimum concentration for Gd concentration, a test block situated with a series of containers was prepared, which has the diameter of 4mm. The Gadolinium to water ratio increased from 0 to 10% for eight containers. The MRI scans were conducted to find the suitable mixing ratio for optimal MRI signal intensity (Figure 4 (a)). It is also equally important to find out the optimum diameter for the Gd container. A test block situated with a series of container of gradual increasing diameters was prepared. The Gadolinium to water ratio was optimized and fixed in this case (Figure 4 (b)).

4.5 OncoNav Software

This software provides additional guidance for the physician to use the template in the MRI environment. After the template is registered with the software, it is able to place artificial markers on the template and further enhance the functionality of projected needle pathway. The software outputs the grid location for needle insertion as well as the insertion angle and depth. (Figure 5).

4.6 Needle Placement Accuracy Test

Three targets were identified and the template was placed in position on the prostate phantom through an MRI scan. The OncoNav software was used to provide essential information on the hole selection and insertion depth. Finally, the needle insertions were performed inside a CT scanner. Overall, 13 insertions were performed on three targets. Figure 6 (a) shows the template setup inside the CT scanner. The insertion accuracy is further analyzed using error bars and Bland-Altman plots.

4.7 Clinical Workflow

The clinical workflow of the proposed template-based approach is designed to be as close to the current biopsy procedure as possible. This will enable the physician to perform the biopsy without significant additional training. The major difference is the template can be registered rapidly with the assistance of OncoNav onto the MRI images, so there is a significant improvement in initial setup time Figure 7.

The detailed workflow is as follows:

1. Place the patient on the support board with standard Lithotomy position inside the MRI scanner.
2. Take the template out of the sterile bag and place it on the perineum of the patient.
3. Scan the prostate tumor region, register the template with the OncoNav software, identify the target on the user interface of OncoNav and select the best location on the template mapping for insertion with the assistance of the virtual needle function.
4. Administer local anesthesia to the area of insertion.

5. Insert the needle through the planned hole, puncture the skin and move towards the tumor by incremental distance, followed by the projected pathway of OncoNav.
6. Take intermittent MRI scans and evaluate the insertion pathway.
7. Readjust the needle position by switching to different insertion hole if the MRI images from intermediate MRI scan shows the needle will miss the tumor target significantly. Step 4 to 6 is repeated until the needle tip is moving towards the tumor on planned pathway.
8. The treatment is started as soon as the needle tip is directly on the target tumor.
9. Steps 4–8 are repeated if multiple insertions are required.

5. Results

5.1 Image Contrast

The test block was used to determine the optimum Gadolinium (Gd) concentration for the template. As can be seen on Figure 8, both the image brightness and the signal intensity reach maximum when the concentration of Gd is 0.9 mg/ml, which corresponds to a 500:1 Gd to water ratio. The test was carried out in a 7T MRI scanner and the sequence used was T1-weighted.

The test block was used to find out the optimum Gd container diameter for the template. The concentration of the Gd solution is 0.9 mg/ml. As can be seen on Figure 9, the image brightness and the signal intensity are the best when the diameter is 5mm. However, due to the size constraint of the template for transperineal needle placement, the maximum container diameter was adjusted to 4mm. The test was carried out in a 7T MRI scanner and the sequence used was T1-weighted.

5.2 Needle Placement Accuracy Test

Figure 10 shows 9 of the 13 insertions being conducted in the phantom study. The total distance (TD) error, superior-posterior (SP) error and left-right (LR) error is displaced at the bottom of each CT image.

The SP, LR and overall distance errors are shown in terms of error bars in Figure 11.

The SP and LR error have been analyzed and Bland-Altman plots are in Figure 12.

6. Discussion

A new method for real-time MRI-guided biopsy with OncoNav software is described. Although a prospective analysis of a large cohort of patients will be required to critically assess the clinical feasibility of this procedure, the ability to target simulated prostate tumors with acceptable accuracy has been demonstrated in a CT phantom study in this paper.

Since the initial development of PSA screening, the pathological diagnosis of prostate cancer has been based on the gold standard-systematic TRUS biopsy. However, the reported

poor sensitivity of such biopsies shows the limitation of this conventional method and raises concerns about potentially missing significant cancer¹⁶. The TRUS-guided prostate biopsy has already been associated with high false-negative test results, which leads to repeated biopsies in men as their PSA levels continue to increase. MRI-guided biopsy, either using fusion biopsy or for in-bore biopsy, has been established as an alternative method of investigating suspicious lesions on MRI. Moreover, the false negative rate of mpMRI has been significantly improved. Pepe et al reported a 16.2% and 39.7% respective false negative rates for targeted fusion prostate biopsy of PI-RADS 3 or greater and 4 or greater lesions²⁸. The mpMRI as well as MRI/TRUS fusion is now widely recognized as one of the most efficient and cost effective methods to detect significant prostate cancer^{8, 26}. Recent studies showed the fusion biopsy detected 30% more high-risk cancers and 17% fewer low-risk cancers²³. In two of the literature, the diagnostic accuracy of in-bore and MRI/TRUS fusion biopsy is 24.4% and 37% respectively^{33, 39}.

The high-resolution and comprehensive image information provided by MRI has proven to be successful in diagnosing more clinically significant prostate cancers and fewer indolent cancer. Thus, it is proposed that there is an opportunity for the physician to benefit further by utilizing a guided system combining both the real-time MRI image with the actual body structure. Compared to transperineal template-guided mapping biopsy (TTMB)³⁶, the MRI-visible template is able to provide accurate positional and inserting depth information. Moreover, the physicians are able to perform needle insertion on optimal skin entry point and adjust the needle pathway to reach the tumor with the assistance of the OncoNav software and intermittent MRI scans.

The template-assisted needle biopsy insertion is done by MRI for clinical procedure. One of the limitations of this study is that the validation test was carried out in CT instead of MRI. CT scan is not part of the clinical workflow. During the CT-guided procedure, intra-operative imaging is not used to adjust needle insertions. Therefore, CT is merely a tool to evaluate the accuracy. CT is used in the accuracy test because it is more accessible than MRI and better at localizing the needle.

The 3D printing material is flexible and highly elastic. In addition, the Formlabs® printer can provide a high printing accuracy of 0.05mm. This allows the design of tight-fit and hightolerance holes for specific needle sizes such as 17 G needles, which are commonly used in clinical practice. In addition, the software OncoNav can provide real-time orientational information of the needle to the physicians. Therefore, once the needle is positioned on the template, the orientation of the needle can be manually adjusted.

The connectors are designed to be removable so that the template not only can be easily segmented into smaller pieces and sizes for different populations, but also can be flexible enough so that it can attach to the skin surface directly. Together with the MRI-visible Gd containers, the template is able to appear as a series of columns along the curvature of the skin surface in MRI images at transverse view.

Due to the proximity of the template, the physician can have an understanding of the distance from the skin entry point to the target. Since the template appears constantly on

MRI slices on both coronal and transverse views, it allows the physicians to visualize the 3D needle trajectory based on the position and orientation of the template. The physician uses the MRI coronal images to determine the best skin entry point. After the needle is inserted, template images at transverse planes provides angular and depth information of the needle. One limitation of the template is that all the markers may not be shown on the single slice of the MRI image, however, OncoNav software is able to register each marker of the template and display both existing and software simulated marker positions. During the insertion, the template stays firmly on the skin surface so that the physicians can take intermediate MRI scans, adjust the needle orientation if it deviates from the planned trajectory or any unplanned occurrences. This can ensure insertion accuracy comparable to the robot-assisted approach without dedicated training. Zandman et al., has developed robotic device with average error 1.84 mm²⁴. Other robotic system like Srimathveeravalli et al has achieved an accuracy of 2.58 mm³⁴. The mean error of the proposed template is 2.7 mm.

The signal intensity is the key for the template to be visible in the scan images. There are four factors influencing the signal intensity; the first is the mixing ratio between Gd solution and pure water, the optimized value is 1ml:500ml. In Figure 8, the pure water appears darker than the rest of the Gd solutions, this is because the higher the Gd concentration, the more quickly the molecules in Gd concentration can realign its longitudinal magnetization with B₀ after RF pulse, thus shortening T₁. Therefore, the image will appear brighter on T₁ weighted scans. On the other hand, the concentration of 42.6 mg/ml is dark because of profound shortening of T₂. The second factor is the size of the Gd container, a larger container will have more visibility in the MRI images. However, because the overall size of template is limited to the perineal region, a larger container will greatly increase the separation distance between the insertion holes. This will reduce the accuracy of the needle insertion process. The third factor is the sequence used during the MRI scanning. A T₁-weighted sequence is used in the MRI scan because it is a standard procedure for experimental purpose in the research institution. In the future, a T₂-weighted sequence will be used so that tumors can be optimally visible. The final factor is the location of the organ. The prostate is closer to the bladder, which will lower the template visibility because of the urine storage.

The uniqueness of the procedure is that the template can be mounted to the patient with a close skin contact. The template is filled with optimized concentration of contrast agent, which is MRI-visible in both transverse and coronal plane. OncoNav software allows the template to quickly register with pre-scanned MRI images. The physician is able to perform the needle insertion with real-time indication of needle position. However, one of the limitations is that the contrast agent will gradually lose its MRI visibility over a month's time due to the vaporization of the solution. We will find out a better way to seal the contrast agent and retain its maximum visibility in the future. The other limitation is that the flexibility could potentially self-introduce some errors because some insertion holes on the template will be slightly stretched on uneven surface. Two solutions are: the OncoNav will provide real-time predicted needle trajectory to ensure the needle stay in the right path and the intermittent scans will further guarantee the needle remains targeting towards the lesion.

In terms of economic potential, the template can be printed out in a 3D printer repeatedly with consistent quality. The print material is flexible phtopolymer resin FLFLGR02

developed by Formlabs®, which is commercially available. Finally, the template is designed to be reusable for a predetermined number of uses and then becomes disposable.

This paper presents an innovative flexible template which can be 3D printed with biocompatible material. The template is designed specifically for the transperineal prostate biopsy in MRI scanners. The template can be cut into customized sizes for different age groups. Other important features are its visibility on MRI and the ability to quickly register it to standard images. The phantom study shows, with the assistance of the template and software OncoNav, the accuracy of the prostate biopsy is comparable to a robotic system. It can be foreseen that the overall clinical procedure time will be reduced without significant alteration of the clinical workflow. Future work will be testing the diagnostic accuracy of the template in a human clinical study and compare the results with standard procedure for needle biopsy.

One of the future developments will be adjusting the hole sizes of the template and allowing tight-fit feature for more selection of biopsy needles. Further tests will be done to explore this new category of prostate needle biopsy. Moreover, using the template as an effective treatment needle guidance for targeted cancer treatment will be under consideration. Another future work will be testing the diagnostic accuracy of the template in a human clinical study and compare the results with standard procedure for needle biopsy.

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Figure 1.
Proposed template-guided system for minimally invasive interventional procedure

(a) CAD drawing

(b) Print result

(c) Flexibility test

(d) Cap design

(e) Assembly result

(f) MR image

Figure 2.

(a) shows the design of the template, (b) shows the 3D print result from the formlabs®, (c) shows the template flexibility test, the template was able to bend and make full contact with the arch. (d) shows the cap design for sealing the contrast agent, (e) shows the final assembly result of the template, (f) shows the MR image (T1-weighted).

(a) Top view of the template

(b) Sideview of the template

Number	Description
(1) Needle insertion point	The holes are suitable for 16, 17 and 18G needles.
(2) GDP container	The diameter is 4mm, the circular design is to ensure the best print result and mechanical stability. A circular cavity opening is more easily covered.
(3) , (5) Connector	It is optimized to be 2mm in length and 2mm in height, this achieves a balance between strength and flexibility.
(4) GDP container	The height is optimized to be 10mm to ensure the best visibility in MRI images period.

Figure 3.
detailed design information on optimization

(a) Test block for Gd concentration

(b) Test block for diameter

Figure 4.

Two different types of test blocks were CAD designed and 3D printed for optimizing both the Gd concentration and container size. (a) shows the circular containers with a constant diameter of 4mm but the concentration of Gd-water solution increases from 0.9mg/ml to 42.6mg/ml and pure water as a control reference is placed at the bottom right corner, (b) shows a series of containers with gradual decreasing size, optimal Gd concentration is applied to all the containers in this case.

(a) Registration in the OncoNav

(b) A virtual needle shown on the template

Figure 5.

(a) shows the registration user interface, the blue dots are manually identified markers, the yellow circles are where the software thinks the MRI contrast should be located, the red dot is the projection of the target on the template, (b) shows the virtual needle generated by the software goes through the interval between fiducial markers.

(a) Template setup in the scanner

(b) Typical needle insertion CT image

(c) Distance illustration

Figure 6.

(a) shows template placed inside the CT scanner, (b) shows the typical CT image, (c) how the distance is measured and analyzed, LR is the left-right distance error, SP is the superior-posterior distance error.

Figure 7.
The clinical workflow of template application

(a) MRI signal of different Gd

concentrations

(b) MRI signal intensity versus Gd concentrations

Figure 8.

(a) shows MRI images of different concentrations of Gd solutions, (b) shows the signal intensity versus the Gd concentrations

(a) MRI signal of different test container diameters

(b) MRI signal intensity versus test container diameter

Figure 9.

(a) shows MRI images of different test container diameter, (b) shows the signal intensity versus the test container diameter

Figure 10.

shows the 9 out of 13 insertions on the prostate phantom are displayed and analyzed. (a)—(c) is on Tumor A, (d)—(f) is on Tumor B and (g)—(I) is on Tumor C.

Figure 11.

shows comparison of absolute values of SP, LR and TD errors for 13 insertions.

(a) For the SP error

(b) For the LR error

Figure 12.
shows the Bland-Altman plot for SP and LR respectively

Table 1:

Existing assistive needle guidance systems

Lead Author	Template type	Dimension	Function	Application
Tokuda J. et. al ³⁷	Acrylic block	100×120×25mm	Biopsy needle guide	Prostate biopsy
Hata N. et. al ¹⁸	Standard template	0.0059-inch holes spaced 5mm apart		
Pinkstaff et.al ²⁹	Standard template	N/A		
Ayres, Benjamin E., et al ³	Virtual template mapping	Brachytherapy template with holes at 5mm intervals		

Table 2:

Commercially available needle guidance systems

Companies	Template type	Size	Function	Application
Civico® ⁷	N/A	N/A	Positioning and stabilizing equipment	CT-guided procedures
Noras® ²⁵	Biopsy unit for GE 8-channel breast coil	N/A	Lateral, medial and cranio-caudal access to the breast	MRI-Breast biopsy
Webb medical ® ⁴⁰	The Fast Find Grid®	N/A	Flexible grid, fast and accurate pinpointing of area	CT-biopsies

Table 3:

Design criteria and descriptions of an ideal needle template

General criteria	Descriptions
Cost	The cost should be significantly lower than the current costs of commercially available templates
MRI-compatible	The material used should be MR-compatible, the quality of scan images should not be significantly impacted by the presence of the template
Optimal SNR	The signal to noise ratio has to be adjusted to be optimum at different image sequences, primarily T1 and T2-weighted.
Environmental hazards	The material should be disposable
Training requirement	The procedure of using the template should facilitate a fast learning curve and be easy to manipulate
Set up requirement	The template should be compatible with the MRI scanner, easy to setup and be quickly adopted into the clinical environment
Site restriction	The template can be used in both a small MRI clinic and a large hospital
Patient accessibility	It should be a flexible template which can be mounted on any skin contour. It should be easily resizable with common scissors to personalized the template to each patient's dimensions.
Patient safety	The material used must be biocompatible. The template has to be properly sterilized before use.
Operational criteria	Descriptions
Size	The dimensions of the template are designed to be fit on the patient's perineal region, the template size can be customized to suit specific patients.
Manual insertion	The insertion holes should be evenly distributed on the template, the separation distance is 8mm
Image contrast	Magnevist® by (Bayer HealthCare Wayne, NJ), a contrast agent used in MRI imaging, the main chemical composition being Gadopentetate Dimeglumine
Patient mounted	The flexibility of template allows being attached to the patient's skin surface. Double-sided tape is added on one side of the template to give the adhesive nature