Int J CARS
DOI 10.1007/s11548-011-0600-6

ORIGINAL ARTICLE

Immobilization and catheter guidance for breast brachytherapy

A. Pompeu-Robinson · M. Kunz · C. B. Falkson · L. J. Schreiner · C. P. Joshi · G. Fichtinger

Received: 10 January 2011 / Accepted: 26 April 2011

Abstract
Purpose Brachytherapy is an important mode of breast cancer treatment; however, improvements in both treatment planning and delivery are needed. In order to meet these specific needs, integration of pre-operative imaging, supplemented by computerized surgical planning and mathematical optimization were used to develop and test an intra-operative immobilization and catheter guidance system.
Method A custom template specific to each patient with optimally placed guide holes for catheter insertion was designed and fabricated. Creation of the template is based on a virtual reality reconstruction of the patient's anatomy from computed tomography imaging. The template fits on the patient's breast, immobilizing the soft tissue, and provides pre-planned catheter insertion holes for guidance to the tumor site. Agar-based phantom and target models were used for quantitative validation of the template by ascertaining the precision and accuracy of the templates.
Results Tests were performed on agar-based tissue models using computed tomography imaging for template planning and validation. Planned catheter tracks were compared to post-insertion image data and distance measurements from target location were used to create an error measure. Initial results yielded an average error of 4.5 mm. Once the workflow and template design were improved, an average error of 2.6 mm was observed, bringing the error close to a clinically acceptable range.
Conclusion Use of a patient-specific template for breast brachytherapy is feasible and may improve the procedure accuracy and outcome.

Keywords Breast cancer · Brachytherapy · Radiotherapy · Immobilization · Guidance

A. Pompeu-Robinson (✉) · M. Kunz · G. Fichtinger
School of Computing, Queen's University, Kingston, ON, Canada
e-mail: robinson@cs.queensu.ca

M. Kunz
Department of Surgery, Queen's University, Kingston, ON, Canada

C. B. Falkson · L. J. Schreiner
Departments of Oncology, Queen's University, Kingston, ON, Canada

C. B. Falkson · L. J. Schreiner · C. P. Joshi
Cancer Center of Southeastern Ontario (CCSEO), Kingston General Hospital, Kingston, ON, Canada

L. J. Schreiner · C. P. Joshi
Medical Physics, Queen's University, Kingston, ON, Canada

Background and clinical significance

Breast cancer is the most prevalent form of cancer in women, with one in nine American's developing the disease during her lifetime [1]. Radiation therapy has become a routine component in the breast cancer treatment regimen.

Until recently, the standard of care for breast cancer was full mastectomy - the complete removal of one or both breasts. This is a very effective treatment method, but this radical surgery is extremely traumatic for the patient, both surgically and esthetically. Lumpectomy has evolved as a more conservative surgical approach, which spares the breast by removing only the tumor and a region of surrounding tissue. The current standard of care consists of a lumpectomy followed by external beam radiation therapy (EBRT) [2]. Delivering radiation externally is dangerous to both skin and vital organs situated near the chest wall. Typically, breast EBRT requires 6–7 weeks and it prompts many patients to rely on simpler and quicker methods of treatment instead. Many patients opt to revert back to radical breast removal surgery.

Published online: 19 May 2011

In contrast to EBRT, brachytherapy involves inserting sealed radioactive sources through hollow catheters into the target tissue, thus radiating the cancer from inside out. Brachytherapy reduces radiation to healthy tissues, especially to skin, while allowing for tight localization of the radiation dose around the tumorous target [3]. The entire breast brachytherapy regimen takes approximately one week. In 2008, the California Technology Assessment Forum performed a comprehensive review on the safety and efficacy of brachytherapy and concluded that, although this treatment could potentially outperform EBRT, studies thus far have been insufficient to draw long-term conclusions [1].

Controlling local disease using radiation therapy depends on delivering adequate full-tumor coverage. Retrospective studies show a strong positive correlation between local recurrence and inadequate coverage [4]. The ability to consistently and reproducibly localize and fully irradiate the tumor site is very important in radiation therapy. Brachytherapy relies on accurate catheter insertion, and so immobilization and guidance are key factors. Patient immobilization has many aspects, ranging from controlling the pose of the body to specific tissue immobilization devices. Positioning of the patient during breast radiotherapy is a heavily debated topic. The patient's arm is usually extended overhead to expose the axilla during EBRT. Positioning the patient in a supine position is the common method for treatment, but the current trend is prone position delivery [5–7]. Popular immobilization devices include thermoplastics, the Kuske breast applicator (Fig. 1), custom-casts, evacuated bead bags, brassieres, and vacuum-sealed devices. Most of the immobilization devices available are used for EBRT. The Kuske breast applicator (Nucletron, Veenendaal, The Netherlands) is currently the only widely used brachytherapy immobilization device.

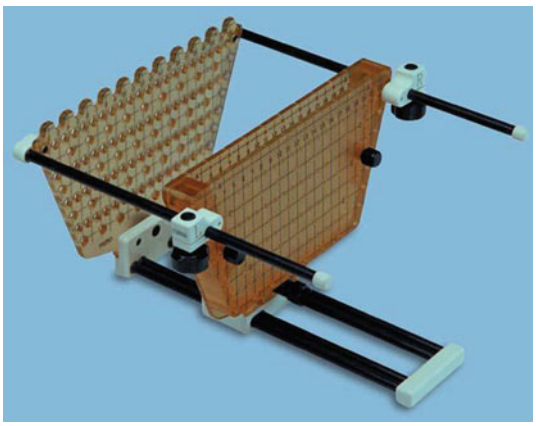

Fig. 1 The Kuske applicator (Nucletron, Veenendaal, The Netherlands) is an adjustable template with integrated guiding plates that are used to compress the breast and guide placement of brachytherapy needles

The purpose of this work is to contribute to the breast brachytherapy protocol. Through the use of patient-specific templates treatment could be performed more effectively and safely, as the template will serve as both an immobilization system and as a guidance system. We believe that the use of patient-specific templates would make breast brachytherapy more accurate, consistent, predictable, and increase patient comfort. These advances should lead to better acceptance of breast brachytherapy among patients and, in the long run, improve clinical outcomes.

Methods

Concept

The goal of this project is to integrate pre-surgical computer plans and create a method of immobilization and guidance. The resulting protocol,which can be viewed in Fig. 2, hopes to eliminate one pre-operative patient visit and improve the comfort of the patients during the procedure. The central idea is using patient-specific custom-made immobilization casts, with embedded guidance holes for the brachytherapy catheters. The surface of the breast can be segmented using pre-operative computed tomography (CT) images and the reconstructed surface used for template creation. The pre-operative CT also allows for the localization of the tumor site. A patient-specific cast encompassing the breast is then printed in three dimensions using a rapid prototype printer. The printed cast also contains pre-planned catheter insertion holes. The concept of patient-specific templates has been investigated in orthopedic surgery [8–14] and neurosurgery [15]. To our best knowledge, there has been no research into adapting this concept for a soft tissue, such as the breast. We propose to extend this concept for breast tissue by implementing a patient-specific template that fits over the breast, immobilizes the soft tissues, and provides insertion holes for guiding the catheters to the tumor sites.

Clinical workflow

The workflow designed for catheter insertion with patient-specific breast brachytherapy template can be viewed in Fig. 2. Clinically, the workflow would be similar to current brachytherapy treatment procedures. However, we hope to remove the need for multiple imaging sessions and to improve patient comfort. In current brachytherapy practice, the patient is first CT imaged to discern the tumor site, and then a catheter insertion plan and a dosimetry plan is created. The patient then undergoes catheter insertion using the Kuske applicator, usually performed under some form of image guidance. Following catheter insertion, the patient undergoes a second CT imaging session to confirm catheter

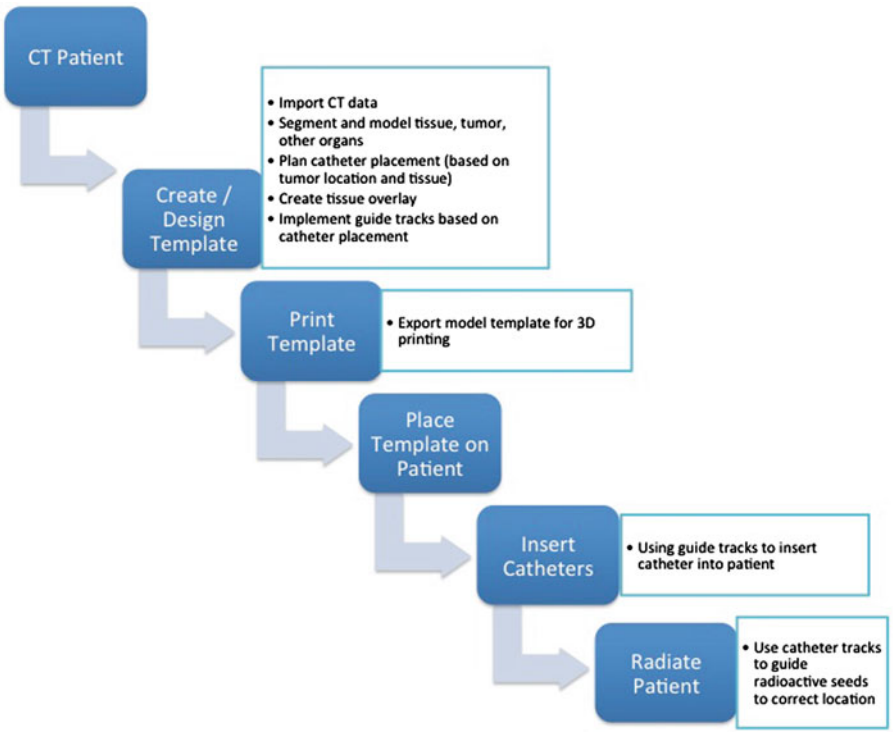

Fig. 2 Clinical workflow of brachytherapy procedure using patient-specific template

locations and update the dosimetry plan. The proposed clinical workflow (Fig. 2) would commence in a similar fashion with CT imaging, catheter planning, and dosimetry. In our case, however, the catheter insertion plan would be incorporated into a patient-specific template. The template would act as an immobilization device for the soft tissue as well as a guidance device for catheter insertion. This would eliminate the need for the Kuske applicator and may obviate the need for intra-operative and post-insertion imaging. Thus, following catheter insertion, irradiation may commence immediately.

Phantom experiment workflow

We created agar-based phantoms with tumor sites in clinically representative locations. The phantom breast tissue was then imaged with CT and visualized using modeling software. The breast and embedded targets were reconstructed in three dimensions and an enclosure that would serve as the template was designed over the breast surface. The catheter trajectories were planned to target the tumor sites (Fig. 3a) and their intersections with the breast surface were identified (Fig. 3b). Guide holes and short guide sleeves were added to the virtual enclosure model (Fig. 3c), resulting in a patient-specific template for breast immobilization and catheter guidance. The virtual template model was printed using a 3D rapid prototype printer. The printed template was placed over the breast and catheters were inserted through the guide holes into the target lesions (Fig. 3d). The tissue, template, and catheters were then all imaged using a CT machine and registration techniques were implemented in order to assess the quality of catheter placement.

Software

Creation of a 3D template and post-surgical validation of inserted catheters requires various visualization and modeling tools. In order to create the patient-specific template, two software tools created by Materialise (Leuven, Belgium) are used. *Mimics* 13.0 and *Magics* 14.01 were used for 3D modeling of the tissue, template creation, and post-operative validation through registration.

Mimics was designed for medical image processing. The processing and editing of 2D image data (CT, μCT, MRI, etc.) are easily and accurately done using Mimics. The construction of 3D models, powerful segmentation tools and measurements tools make this a strong platform for medical image analysis. Mimics can also easily export your 3D data to a wide range of output formats.

Magics is a rapid prototyping software that allows for the importing of various modeling formats as well as easy exporting for rapid prototype printing. Magics contains a variety of modeling tools for 3D model creation, optimization, parts analysis, and repair. We choose these tools because they have been used extensively in the field of patient-specific guide design [8–11,14].

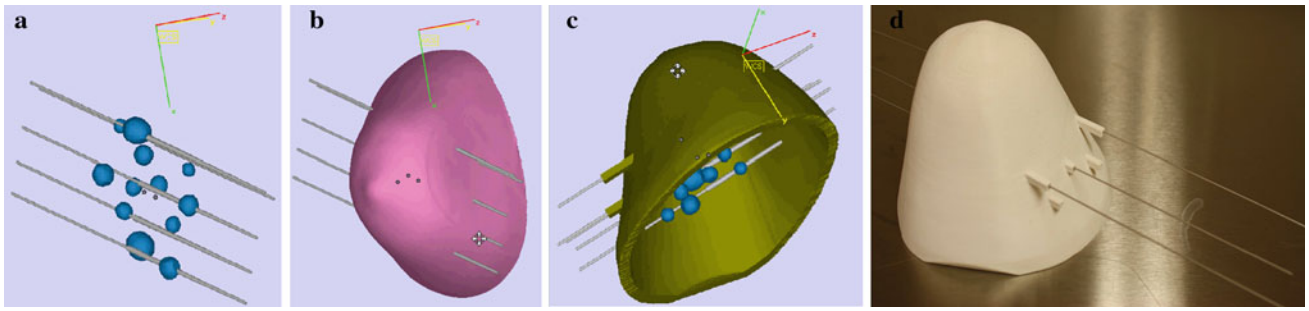

Fig. 3 **a** Catheters planned to target embedded tumors. **b** Catheters in relation to reconstructed breast. **c** Template with catheters targeting embedded tumors. **d** Printed template with catheters running through the guide holes

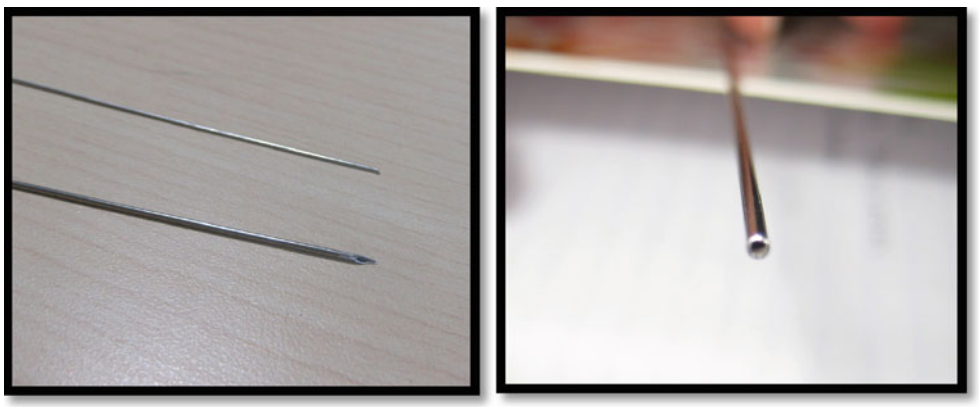

Fig. 4 *Left* Catheter on *bottom* and needle analogue on *top*. *Right* Close-up image of catheter analogue

Catheter analogue

To evaluate the validity of a patient-specific template on soft tissue, multiple experiments are needed to show significance, with inserting a very large number of brachytherapy catheters. As clinical-grade supplies are rather expensive, a suitable analogue of 18-gauge catheters and needles were created as seen in Fig. 4. Twelve precision miniature stainless steel-welded and drawn tubing sized at 18 GA were purchased to simulate the brachytherapy catheters. Miniature stainless steel drive shafts with an outer diameter of 1/32" and a length of 12" were purchased to represent the needle that usually runs through the catheter.

Breast tissue analogue

In order to validate the feasibility of patient-specific template, artificial breast tissue models, also known as phantoms, were created using agar and gelatin. Combining 80 parts water, 2 parts agar, 4 parts gelatin, and 1 part glycerol over a hot plate makes a suitable tissue substitute that can be imaged easily with CT and, if necessary, with ultrasound. Once the water is heated to 75°C, the agar and gelatin are slowly added to avoid clumping. The glycerol is added after all the agar and gelatin have dissolved fully. The mixture is then stirred to ensure proper incorporation of the glycerol and then left to cool to 50°C. The mixture is then poured into breast molds and left to set in refrigerator for at least 12 h. To simulate a tumor site, the tips of agar-filled latex gloves were placed into the breast phantoms prior to cooling at random locations to mimic reality.

Template

From pre-operative CT imaging, the patient's anatomy including the breast surface, tumor, and surrounding structures are graphically reconstructed in three dimensions on a computer. The optimal position of the catheters is computed to provide optimal dose coverage of the tumor. In a virtual reality computer interface, a template mask is designed to cover the breast surface with guide holes for the catheters. Finally, the template is printed using 3D rapid prototyping technology. Upon sterilization, the template is placed on the patient's breast and the surgeon inserts the catheters through the guide holes.

The key to the proposed technique is using the patient's anatomy to create a comfortable immobilization device and

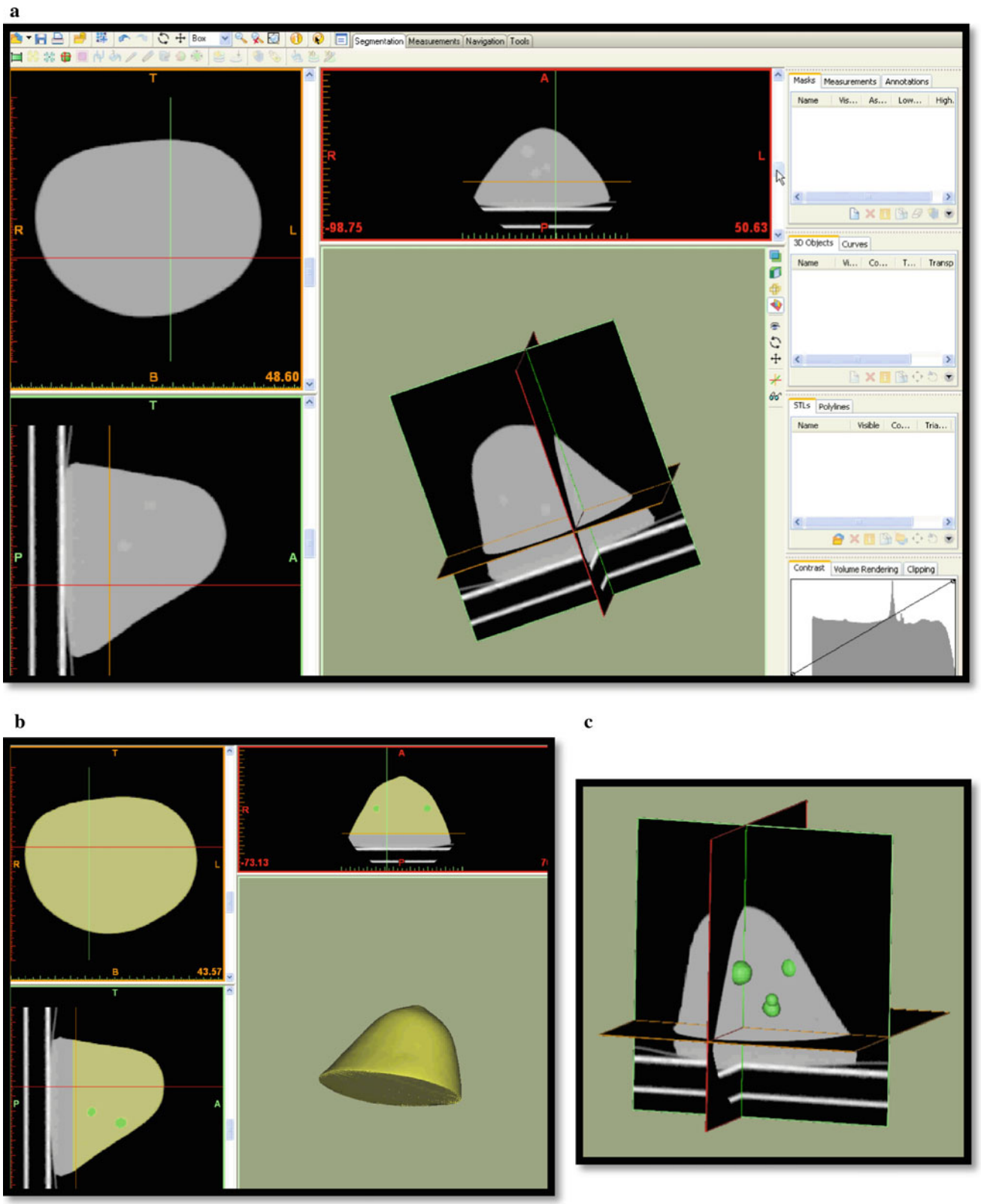

Fig. 5 Screen shots from *Mimics*. *Top* **a** shows the layout of *Mimics* right after importing CT images of the breast tissue. *Mimics* has three screens showing different views of the tissue and one screen incorporating all views into a 3D visualization. *Bottom Left* **b** segmented breast tissue (yellow) and 3D rendered model of breast. *Bottom Right* **c** 3D rendered model of segmented tumor sites (green)

incorporating catheter guidance. The initial analysis of CT image data is first rendered with the *Mimics* software. The design of the patient's specific template is achieved with using the *Magics* software tool, the output of which is then exported for 3D printing.

The template is created during the pre-operative stage of our workflow and requires 3D imaging of the tissue. The data retrieved from using CT to image the agar phantom are loaded into *Mimics* (Fig. 5a). *Mimics'* segmentation tools are used to discern the tissues contour, vital organs, and tumor site (Fig. 5b). Using the software, a 3D model of the segmented areas (Fig 5c) can be created and exported in a modeling format for processing and template creation in *Magics*.

The model of the tissue and tumor site is then loaded into *Magics*. Creation of catheter models in *Magics* is done so as to visualize how treatment should be given to the tissue (Fig. 3a,b). The modeled catheters are then placed with clinically feasible trajectories to cover the tumor sites (Fig. 3a). A template is then created using the tissues contour as a guide so that the template will fit snuggly over the imaged tissue (Fig. 3c). The catheter insertion sites are then hollowed out on the template so as to create guides for the catheters. Initial tests used a simple hollowed-out section in the template as guides as seen in Fig. 6a. Improvements in the design led to using longer guide tubes for the needles (Fig. 6b) which resulted in reduction of catheter insertion errors. The template is then exported for rapid 3D prototype printing.

Experiments and results

In order to properly validate the use of patient-specific templates for brachytherapy catheter insertion, one must show that the pre-planned catheter tracts and post-operative catheter tracts are sufficiently close. In pre-operative template planning, catheter tracts are created as discussed above. Following insertion of the catheters, the phantom, template, and catheters are imaged in CT. The images are loaded into *Mimics* allowing for 3D rendering of the phantom, template, and needles. The pre-operative breast tissue is registered to post-operative breast tissue using a *Mimics* registration tool that minimizes the least squares distance. Once the pre-operative and post-operative breast tissues are registered, the transformation matrix used for alignment is then applied to the post-operative needles and template. These steps are required for proper comparison of the pre-operative and post-operative needle tracts. A visual inspection of the needles is made first, and a quantitative measure is also taken from the data. The motivation of placing the catheters is to target certain tumor sites. A measure of the distance from the expected catheter site is used as a measure of error.

In order to characterize how accurately the catheters are placed, the distance from pre-planned catheter target locations was used to determine error. The experimental workflow was performed twice. The first test contained two phantoms of average size. Each phantom in the first experiment had five needles planned and inserted. In the first breast phantom, one of the five needles inserted exited the pre-planned exit-hole, leaving four needles butting against the templates edge. In the second breast phantom, two of the five needles passed through the breast tissue and exited through the corresponding hole. The average needle trajectory placement error (shown in Table 1) in the first experiment was 4.83 mm and 4.18 mm, for the two phantoms, respectively. Large variations in targeting error were observed with the largest error at 10.07 mm and the smallest error being 1.95 mm. It was observed that positioning of the template post-printing caused potentially large errors. The template was being placed over the tissue, but rotation and slight tilting of the template as seen in Fig. 7b was causing large errors in catheter placement. The inability of all the needles to pass through the tissue and exit appropriately out of the template showed an error in needle placement through the template. A slight rotation during insertion of the needle was taking place.

To reduce positioning problems, the second experiment's template design and workflow were modified. The addition

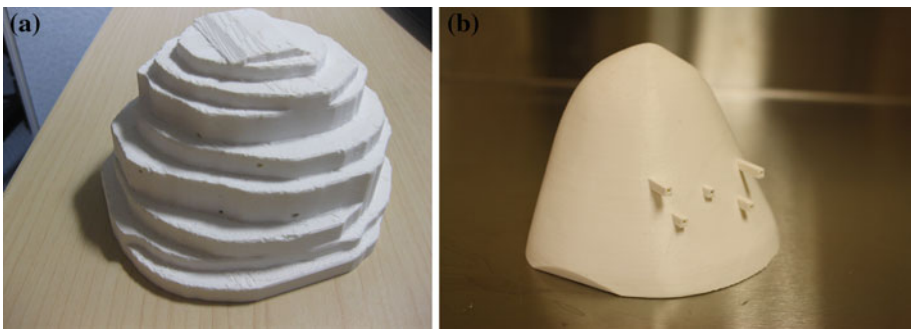

Fig. 6 Templates created using 3D rapid prototype printer *Left* **a** first template designed and printed for catheter guidance. *Right* **b** template printed during second round of experimentation with improvements to template made

Table 1 Distance from target—error measure (mm)

		Needle 1	Needle 2	Needle 3	Needle 4	Needle 5	Average error
Experiment 1	Breast 1	5.34	3.63	4.96	8.18	2.03	4.83
	Breast 2	3.98	1.75	10.07	1.95	3.15	4.18
Experiment 2	Plus	4.59	2.26	2.48	0.96	–	2.57
	Small	2.30	2.84	–	–	–	2.57

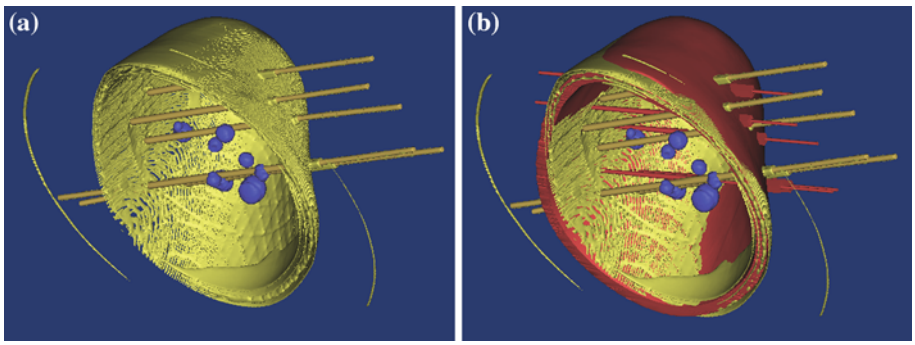

Fig. 7 Screen shots from *Mimics*. *Left* **a** post-operative 3D rendering of tumors (blue), template (yellow), and needles (yellow) created for CT. *Right* **b** post-operative 3D rendering (yellow) with pre-operative template and needles (red) overlaid after transformation was applied. Shows the error incurred from male placement of the template (yellow)

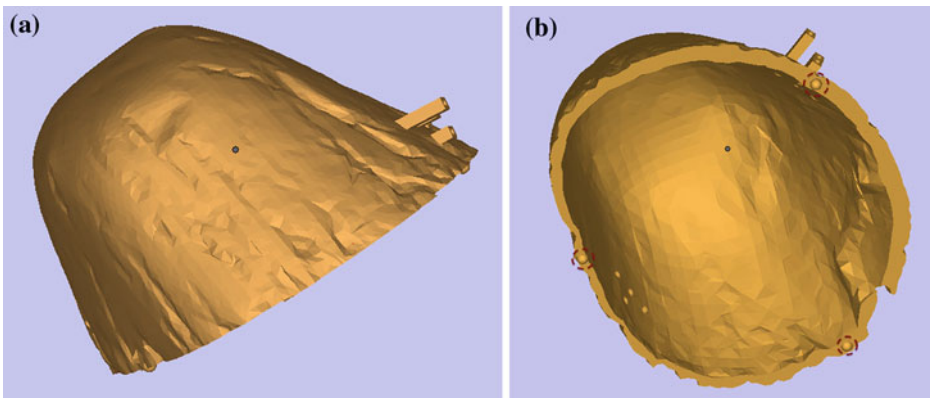

Fig. 8 Screen shots from *Magic*. Model of pre-operative template plan ready for printing. *Left* **a** shows the lengthened guide tracks implemented on template. *Right* **b** displays guide tracks as well as three fiducial guides that appear as spherical bumps along the bottom edge of the template

of three fiducial markers to the breast tissue was incorporated to the workflow to improve template placement. The template itself was improved by incorporating a longer needle guide as seen in Fig. 6 to reduce the needles rotational freedom. Guides were also placed along the bottom of the template (Fig. 8b) for alignment of the device over the skin fiducials placed on the tissue.

Two phantoms of differing breast size (1 plus size and 1 small) were used in the second experiment. Four needles were placed in the plus-size breast yielding an average error of 2.57 mm, with 2 of the needles not exiting the encasing. The small breast was only given two needles due to size constraints, both of which passed all the way through the template, resulting in an average error of 2.57 mm.

A marked improvement between the first and second experiment can be seen. The average errors for each phantom in the second experiment were almost half that of the first two phantoms. The variation in error measures was also greatly improved with most of the errors lying in the same range in the second experiment, while the first experiment produced variations of up to 8.32 mm in error measures. The small changes made in template design and workflow greatly improved the overall outcome of the results.

Future work will improve the workflow, fiducial, and template designs. We will also experiment with changing the shape and dimension of the needle exit-hole. In order to establish precision for this technique, a comparison of the magnitude of errors over multiple tests need to be analyzed, but unfortunately, the project has not progressed to the point of yielding enough data points for the analysis of precision.

In conclusion, we introduced an alternative immobilization and guidance device for breast brachytherapy catheter placement and demonstrated the concept of patient-specific

catheter template guidance integrated with image-based computer-assisted catheter planning. Small changes applied to template and workflow designs yielded major improvements with current results approaching clinically acceptable accuracy. Ongoing work is aimed at improving the workflow and template design while generating more experimental data involving a variety of breast phantoms and eventually human subjects.

Acknowledgments This work has been supported by US National Institutes of Health, 1R01CA131363-01. We are grateful to Randy E. Ellis, PhD for guidance in the early phase of the project.

Conflict of interest None.

References

1. Tice JA (2008) "Brachytherapy as primary radiation following breast-conserving surgery for stage i or ii breast cancer". Tech Rep. California Technology Assessment Forum
2. Wong R, Ngan RKC, Tang F (2005) Wide-volume partial breast interstitial brachytherapy alone after lumpectomy in breast-conserving treatment for early breast cancer. J HK Coll Radiology 8:256–260
3. Devlin PM (ed) (2007) Brachytherapy Applications and Techniques, ch Breast Brachytherapy. Lippincott Williams and Wilkins, Philadelphia, PA
4. Verhey LJ (1995) Immobilizing and positioning patients for radiotherapy. Semin Radiat Oncol 5(2):100–114
5. Mitchell J, Formenti SC, DeWyngaert JK (2010) Interfraction and intrafraction setup variability for prone breast radiation therapy. Int J Radiat Oncol Biology Phys 76(5):1571–1577
6. McKinnon R, Christie D, Peres H, Burke M, Le T, Lah M (2009) The Breast 18(1):30–34
7. Kudchadker R, Ha C, Stokes C, Kirsner S, Wilder R (2006) "2834: Breast dose reduction in women undergoing mediastinal radiotherapy using a custom prone immobilization device". Int J Radiat Oncol 66(3, Supplement 1), S679–S679. Proceedings of the 48th annual meeting of the American society for therapeutic radiology and oncology, 48th annual meeting of the American society for therapeutic radiology and oncology
8. Hafez MA, Chelule KL, Seedhom BB, Sherman KP (2006) Computer-assisted total knee arthroplasty using patient-specific templating. Clin Orthop Relat Res 444:184–192
9. Kunz M, Rudan JF, Xenoyannis GL, Ellis RE (2010) Computer-assisted hip resurfacing using individualized drill templates. J of Arthroplast 25(4):600–606
10. Owen BD, Christensen GE, Reinhardt JM, Ryken TC (2007) Rapid prototype patient-specific drill template for cervical pedicle screw placement. Comput Aided Surg 12(5):303–308
11. Lu S, Xu YQ, Zhang YZ, Xie L, Guo H, Li DP (2009) A novel computer-assisted drill guide template for placement of C2 laminar screws. Eur Spine J 18:379–1385
12. Radermacher K, Portheine F, Anton M et al (1998) Computer assisted orthopaedic surgery with image based individual templates. Clin Orthop Relat Res 354:28–38
13. Berry E, Cuppone M, Porada S et al (2005) Personalised image-based templates for intra-operative guidance. Proc Inst Mech Eng 219:111–118
14. Lombardi A, Berend K, Adams J (2008) Patient-specific approach in total knee arthroplasty. Orthopedics 31(9):927–930
15. Rajon DA, Bova FJ, Chi YY, Friedman WA (2009) Rapid fabrication of custom patient biopsy guides. J Appl Clin Med Phys 10(4):2897