

Interactive knee cartilage extraction using efficient segmentation software: Data from the osteoarthritis initiative

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Abstract. In medical image segmentation, manual segmentation is considered both labor- and time-intensive while automated segmentation often fails to segment anatomically intricate structure accordingly. Interactive segmentation can tackle shortcomings reported by previous segmentation approaches through user intervention. To better reflect user intention, development of suitable editing functions is critical. In this paper, we propose an interactive knee cartilage extraction software that covers three important features: intuitiveness, speed, and convenience. The segmentation is performed using multi-label random walks algorithm. Our segmentation software is simple to use, intuitive to normal and osteoarthritic image segmentation and efficient using only two third of manual segmentation's time. Future works will extend this software to three dimensional segmentation and quantitative analysis.

Keywords: Interactive segmentation, Knee cartilage, Magnetic resonance image, Random walks, User interface

1. Introduction

Medical image segmentation could be achieved through manual, semi-automated and automated methods. Manual segmentation is straightforward and common in clinical researches [1–3]. However, manual object outlining is resource-intensive, time-consuming and prone to human error [4]. Automated segmentation techniques can expedite the extraction process by eliminating laborious human

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intervention. Nonetheless automated methods fail to segment highly complicated medical images [5–7] because they are required to comply rigid constraints.

In interactive segmentation, the users can replace the manual segmentation by inserting prior knowledge in the form of bounding box [8], seeds (labels) [9,10] or brush [11] into the image. Application of interactive segmentation tools has been wide. Segmentation tools, equipped with various types of semi-automated segmentation algorithms [5,10,12,13], have been developed to solve segmentation problems faced by different kinds of medical images and human body parts. The prospective of interactive segmentation tools for medical image is encouraging [14].

Knee cartilage segmentation is typically challenging because of the thin cartilage structure [15–17] and inferior tissue contrast [18,19]. In particular, closely packed knee joint [20] consists of multiple functioning tissue components such as bones, patellar cartilage, hyaline cartilage, articular cartilage, anterior cruciate ligament (ACL), posterior cruciate ligament (PCL), gastrocnemius muscle, soleus muscle, and infra-patellar fat pad (Hoffa fat pad). The cartilages share ambiguous boundaries with surrounding tissues and can easily misleads the segmentation algorithm [21,22]. Besides, complicated osteoarthritic cartilage [23] deforms arbitrary when osteoarthritis progresses [24]; causing automated cartilage segmentation to fail.

In this paper, we have developed 2D interactive segmentation software for knee cartilage extraction. All editing functions within the proposed segmentation software were developed using MATLAB (Mathworks, Natick, MA). The purpose of this study was to evaluate the efficiency and intuitiveness of this segmentation software and to compare its performance to manual segmentation.

2. Related works

We have reviewed relevant works in segmentation software for knee bones and cartilages in automated and interactive approaches. [25] first obtained a bone-cartilage interface (BCI) using bone statistical shape model and then extracted the cartilage from the BCI based on modified tissue classification method introduced by [26]. Although the authors claimed that their segmentation software was fully automated, the bone statistical shape model atlas was created by manual segmentation. Besides, accurate registration between atlas and testing image was compulsory and this procedure could induce heavy computational burden. Furthermore, active shape model did not consider large variability of osteoarthritic cartilage. Lastly, segmentation result refinement was not possible because there was no such option discussed in their works.

Another automated knee cartilage segmentation tool using multi-atlas approach has been proposed by [24]. The authors were inspired by improved performance of brain segmentation when using multi-atlas method. The multi-atlases of 6 patients were segmented manually using CiPAS (IMITEK, S.C., Monterrey, NL, Mexico) and the cartilage was then obtained through tissue voxel classification method. Similar to [25], this automated method seemed to be relatively inflexible and the multi-atlases creation could be even more arduous when large dataset was used. Hence, we believe that automated segmentation techniques are far from satisfying because laborious manual segmentation remains indispensable and the rigid statistical shape model is unsuitable for osteoarthritic image.

As a result, some works on interactive segmentation have been introduced. [21] produced a 2D semi-automated cartilage segmentation software that combined both expert guidance and computer vision. This segmentation software was intuitive because the users only needed to insert seeds near cartilage edge and the edge detection algorithm will track cartilage edge automatically. Since weak

boundaries between cartilage and bone were common problems, additional editing tool was developed to refine the segmentation result until satisfactory outcome was achieved.

[4] proposed a 2D interactive segmentation tool using Graph Cuts. Unlike [21], interactive method developed by [4] involved more human intervention in the form of scribble. The users would scribble on area of interest and let the Graph Cut algorithm to extract both bone and cartilage. Nevertheless, Graph Cut only allowed two different types of labels at one time [27]. An interesting feature from [4] was the seed propagation feature to propagate scribbles into subsequent image. Besides, revision of seeds allowed swift correction of segmentation result when erroneous seeds have been detected. This feature was highly recommended in real time segmentation practice.

3. Materials and methods

3.1. Identification of important user interface properties

To achieve effective cartilage segmentation, adaptive user guidance should replace rigorous prior models. Instant amendment to unsatisfactory results should be performed intuitively while the proposed software must be fast and simple enough for the users to use. In summary, three pivotal features have been highlighted: convenience, intuitive, and speed. Definitions of these features are elucidated in the following sub-sections:

1. Convenience: This feature illustrates the flexibility to the users to infuse their intention at will. Automated segmentation tools proposed by [25] and [24] did not allow the users to intervene amid the segmentation procedure. The only option to improve the result was to include more atlases to increase the reliability of the system. Interactive segmentation tools, on the other hands, allow the users to insert or remove any types of seeds momentarily.
2. Intuitive: To provide dynamic feedback between human interaction and computer system, the software design must be sensitive to users' usage behavior. Most users would prefer software that could be understood easily. Advanced interactive segmentation tools [28] with too many functions could confuse the user and hinder effective use of the software. Our segmentation tool is designed to be simple but still consists of all necessary editing tools. For example, important editing functions such as drawing tool (Draw), removal tool (Eraser), magnifier (Zoom-in/ Zoom-out) and navigator (Pan) were developed to assist the users in completing the segmentation in straightforward fashion.
3. Speed: Invariably, the efficiency of manual segmentation is hampered by tremendous effort to extract thin and irregular cartilage region. Interactive segmentation only requires the users to roughly insert seeds inside the region of interest and the random walks algorithm will replace human intervention to perform the segmentation. This approach is presumably faster than strenuous human attempt.

3.2. User interaction

The button design of our software is shown in Figure 1(a) and the user interface in pre-segmentation stage is shown in Figure 1(b). There are 6 necessary buttons: Open, Clear, Run, Draw, Erase and Show Result. For the ease of readers, we have simplified the function of every button inside the software. Besides, 5 different types of seed labels i.e. femoral cartilage, tibial cartilage, patella cartilage, bone

and background seeds are available to indicate different objects in the image. Lastly, the Weight text box allows the users to insert preferable beta parameter required by random walks algorithm.

The function of every button is explained in the following section:

Open: This button enables the users to access to the medical image. We utilized the Matlab built-in function `dicomread` to read the MR image of knee. Besides DICOM (Digital Imaging and Communications in Medicine) formatted image, digital image format types such as JPEG, TIFF and PNG are also permitted in our software.

Clear: This button removes all scribbles inside the axes by returning all seeds' index into empty matrix. The objective of this button is to initialize another round of scribbling if the user is not satisfy with current scribble patterns in early stage of scribbling.

Run: This button computes the random walks algorithm. For instance, segmentation is performed after initial round of scribbles has been completed. If the user found the initial segmentation result to be undesirable, refinement is performed and the algorithm is computed again.

Draw: This button enables the users to perform scribbles inside the image according to the users' intention. After the image is loaded into the software, the user usually starts to scribble inside the cartilage. Because random walks algorithm is a multi-label segmentation method, the user needs to specify seed labels to be inserted on the image before the user can start scribbling. The user just needs to right-click on the mouse to terminate the function.

Erase: The objective of erase is to delete selected part of the scribble particularly when Clear button is not an option during refinement stage. To perform the erase function, the user is required to select this button and overlap the wrong scribble with white line. After that, the user can right-click on the mouse to terminate the erase function.

Show Result: The segmentation result would be displayed after Show Result button is selected.

Additionally, this software is equipped with Zoom-in, Zoom-out and Pan functions, which are located at the upper right of the software interface. The usability's of these functions are explained in the following section:

Zoom-in and zoom-out: Contact areas between cartilages are narrow, thus magnifying those obscure areas could help evaluate the image accurately. These two functions were developed using Matlab built-in toolbar editor.

Pan: The hand-like symbol is design to facilitate the zoom-in and zoom-out functions. Developed using the Matlab built-in toolbar editor, this function helps to navigate throughout the enlarged image after zoom-in.

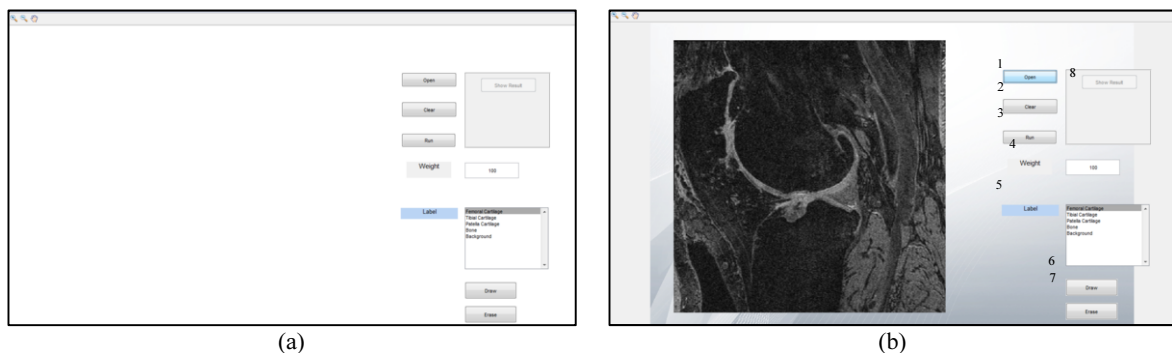


Fig. 1. (a) Button design inside the interface. (b) Pre-segmentation stage and positions of various buttons inside the software: Open button (labeled as 1), Clear button (labeled as 2), Run button (labeled as 3), Weight text box (labeled as 4), Label selection (labeled as 5), Draw button (labeled as 6), Erase button (labeled as 7) and Show Result button (labeled as 8).

3.3. Multilabel knee cartilage segmentation

Random walks algorithm for interactive image segmentation [10] was introduced by Leo Grady. The gist of this algorithm lies with the idea to compare the probabilities that an unseeded pixel belongs to seeded pixel with different labels and select the highest probability. Thence, random walks algorithm is robust to noise and can extend easily to an arbitrary number of labels [29]. Assume an image as a graph with fixed number of vertices and edges i.e. $G = (V, E)$ where $v \in V$ represents the vertices (node) and $e \in E \subseteq V \times V$ represents the edge. An edge spanning two vertices, v_i and v_j is denoted by e_{ij} and the edge's weight is denoted by $w(e_{ij})$ or w_{ij} . The degree of a vertex is denoted as $d_i = \sum w(e_{ij})$ for all edges e_{ij} incident on v_i .

The probability that a random walker first reaches a seeded pixel is equivalent of the solution to Dirichlet problem. Typically, Dirichlet problem can be solved by minimizing the Dirichlet integral subjected to pre-defined boundary condition as shown in Eq. (1). Hence, identifying a harmonic function that satisfies the Laplace equation $\nabla^2 u = 0$ is crucial to the formulation of Dirichlet solution.

$$D[u] = \frac{1}{2} \int_{\Omega} [\nabla u]^2 dV \quad (1)$$

Boundary conditions at the labeled seed points are fixed to unity while seed points with other labels are set to zero. The edge weights and vertex degree are stored in laplacian matrix L as shown in Eq. (2).

$$L_{ij} = \begin{cases} d_i & ; \quad \text{if } i = j \\ -w_{ij} & ; \quad v_i, v_j \text{ are adjacent vertices} \\ 0 & ; \quad \text{otherwise} \end{cases} \quad (2)$$

Then, laplacian matrix is divided into 4 parts and every entry in the matrix, L_{ij} is shown in Eq. (3).

$$L = \begin{pmatrix} L_m & B \\ B^T & L_u \end{pmatrix} \quad (3)$$

where m and u show marked (labeled) and unmarked (unlabeled) pixels respectively. The B matrix is part of the laplacian matrix corresponding to the labels. Solution of the Dirichlet problem is computed by solving the linear system of equations $L_u X = -B^T m$. The L_u indicates edge weights for the unlabeled pixels, m indicates the set of labels for the seed points, B^T indicates the edge weights corresponding to the labels and X indicates the probability for each pixel being a member of the labels. The Matlab code for random walks algorithm is available at <http://cns.bu.edu/~lgrady/software.html>.

4. Experiments and results

We have tested the segmentation software using 10 normal and chronic osteoarthritic (Kellgren-Lawrence grade=3 and 4) dual echo steady state (DESS) MR knee images with water excitation (we). Two observers were involved to compare the manual segmentation using OSIRIX (Pixmeo, Geneva, Switzerland) with the proposed software in terms of intuitiveness and efficiency. The MR images of knee were acquired by using 3.0T MRI scanner (Siemens Magnetom Trio, Erlangen, Germany) with quadrature transmit-receive knee coil (USA Instruments, Aurora, OH) [30]. All DESS images have section thickness of 0.7mm and an in-plane resolution $0.365 \times 0.456 \text{ mm}^2$ (field of view = 140×140 mm, flip angle = 25° , TR/TE = 16.3/4.7 msec, matrix size = 384×384 mm, bandwidth = 185 Hz/pixel) [31]. More information regarding the Osteoarthritis Initiative (OAI) dataset can be found at <http://oai.epi-ucsf.org/datarelease/About.asp>.

Figure 2 describes the convenience feature of our segmentation software. The user needs to specify the type of label from the Label selection box and press Draw button. Then, user can scribble on the image. Seeds in form of scribble will display in different colors (to help differentiate among different types of seed labels) and their spatial locations are stored inside the software. Once completed, user can press Run button and Show Result button to generate the results. We also describe the usage of Erase button and magnification functions (Zoom-in and Zoom-out) during the scribbling process in Figures 3 and 4, respectively.

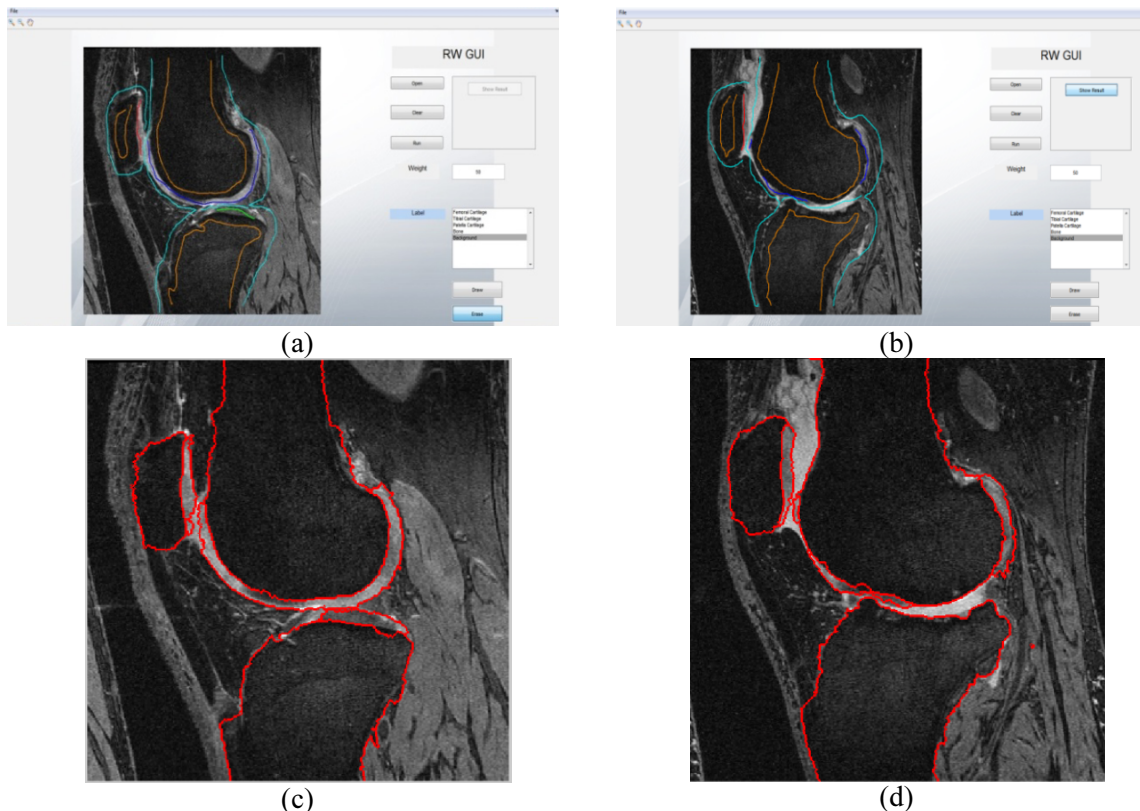


Fig. 2. Demonstration of software convenience and robustness to normal MR image of knee in (a) and osteoarthritic MR image (b) using dynamic scribbling. Segmentation results of both types of images are exhibited in (c) and (d), respectively.

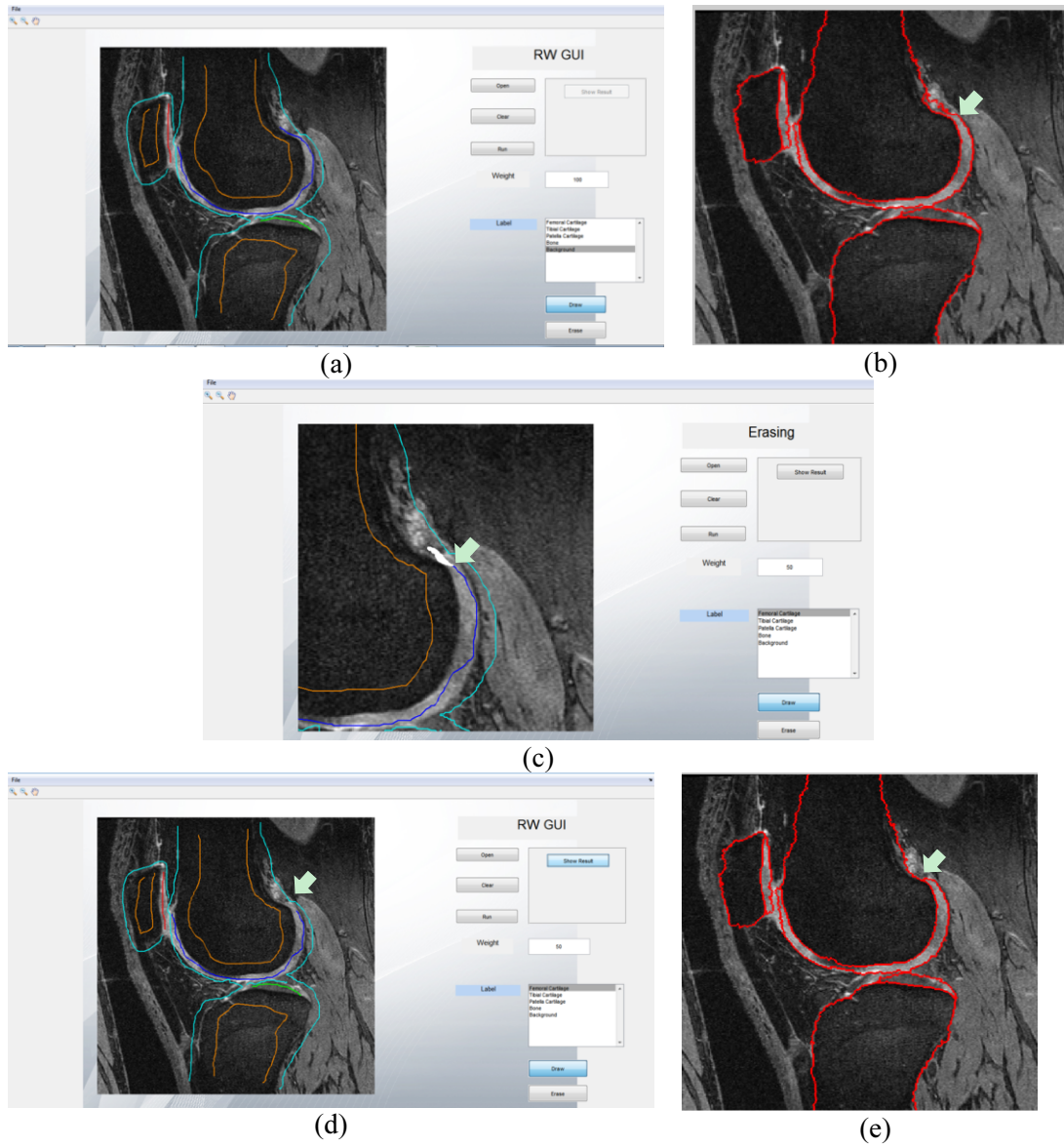


Fig. 3. Procedures to implement Erase function. (a) Original scribble on the MR image of knee. (b) Over-segmentation has been detected at posterior of femoral cartilage (pointed by white arrow). (c) Erase function is applied onto excessively drawn region. (d) Refined scribble after implementation of erase function (e) Segmentation result after the refinement.

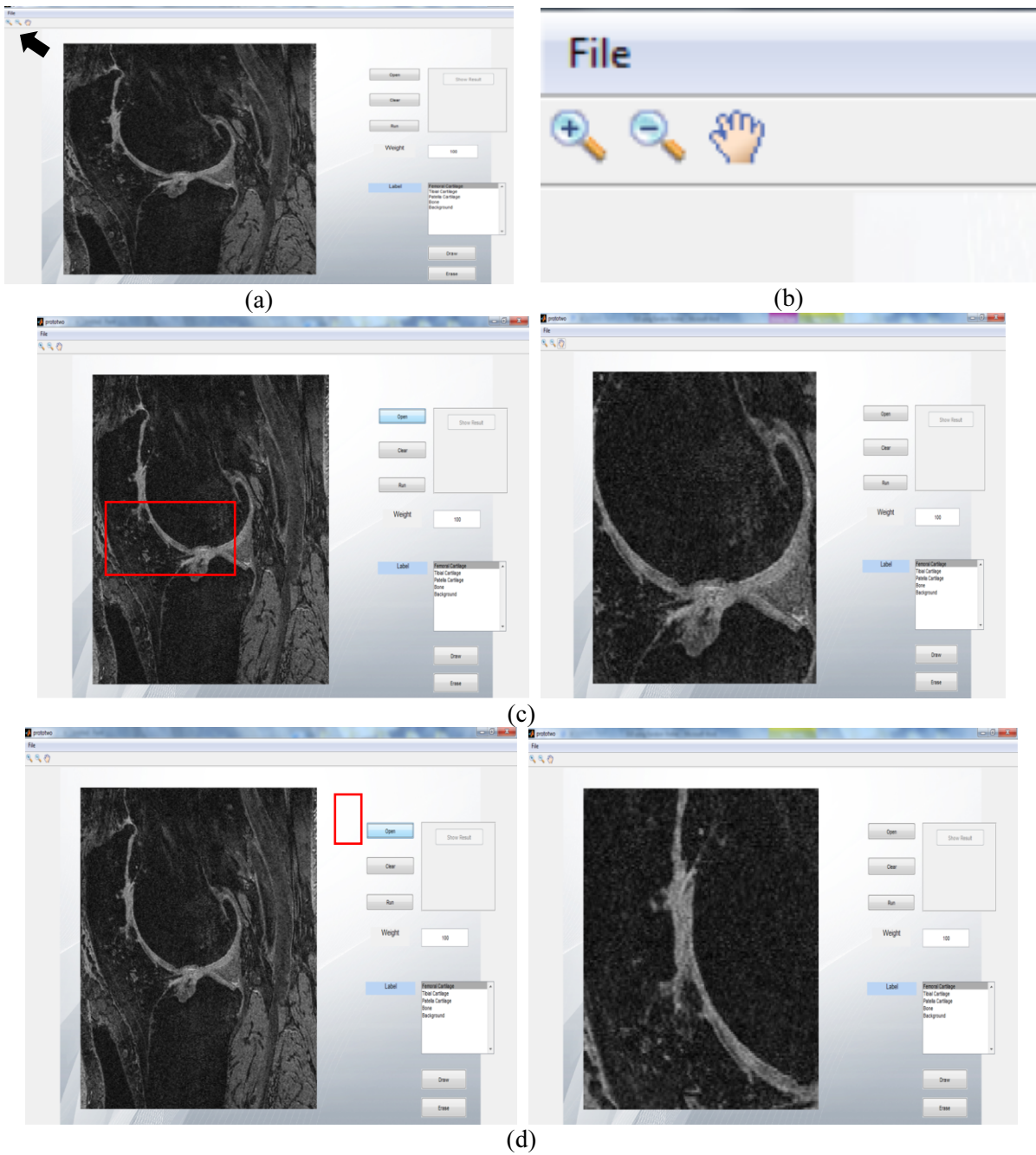


Fig. 4. Procedures to implement magnification function. (a) The magnification function is located at the upper left corner of the software (indicated by black arrow). (b) Select Zoom-in to magnify, Zoom-out to scale back and Pan to navigate. Click on targeted parts (c) femorotibial sulcus and (d) patellofemoral sulcus for magnified views.

Table 1
Comparison of numbers of clicks using various functions in 10 normal images and osteoarthritic images

Functions	Observer 1		Observer 2	
	Normal	Osteoarthritic	Normal	Osteoarthritic
Open	10	10	10	10
Clear	6	3	3	3
Run	17	21	17	17
Erase	4	3	1	2
Label				
• Femoral Cartilage	11	18	10	15
• Tibial Cartilage	12	12	10	10
• Patella Cartilage	11	8	11	9
• Bone	30	30	31	29
• Background	37	55	43	52
Zoom-in	15	22	14	13
Zoom-out	15	22	14	13
Pan	24	20	20	18
Show Result	17	21	17	17
Total Clicks	209	245	201	208

Table 2
Recorded computational time by manual segmentation and the proposed software using normal images

Subject	KL grade	Observer 1		Observer 2	
		Manual	Interactive	Manual	Interactive
9081362	0	5 min 30 s	2 min 11 s	3 min 04 s	2 min 34 s
9109448	0	5 min 36 s	5 min 01 s	3 min 11 s	2 min 35 s
9172459	0	7 min 47 s	2 min 52 s	3 min 46 s	3 min 00s
9222916	0	5 min 01 s	1 min 33 s	3 min 17 s	2 min 40 s
9239017	0	5 min 04 s	2 min 40 s	4 min 30 s	3 min 10 s
9268052	0	4 min 31 s	3 min 15 s	4 min 07s	2 min 18 s
9305272	0	5 min 24 s	2 min 03 s	3 min 58 s	3 min 20 s
9325745	0	3 min 32 s	2 min 29 s	4 min 28 s	2 min 42 s
9357383	0	3 min 10 s	2 min 51 s	4 min 20 s	3 min 07s
9403165	0	5 min 11 s	3 min 04 s	4 min 21 s	2 min 00s
	Averaged time	5 min 05 s	3 min 03 s	3 min 54 s	2 min 45 s

Table 3
Recorded computational time by manual segmentation and the proposed software using osteoarthritic images

Subject	KL grade	Observer 1		Observer 2	
		Manual	Interactive	Manual	Interactive
9047800	3	7 min 00 s	4 min 07 s	4 min 31 s	3 min 40 s
9057150	4	5 min 02 s	3 min 44 s	4 min 57 s	2 min 55 s
9068453	3	6 min 08 s	3 min 15 s	4 min 43 s	2 min 32 s
9102858	3	6 min 12 s	4 min 00 s	4 min 35 s	2 min 56 s
9173013	4	5 min 06 s	3 min 14 s	4 min 01 s	2 min 48 s
9188806	3	5 min 20 s	3 min 54 s	4 min 28 s	2 min 28 s
9279291	3	4 min 39 s	2 min 51 s	3 min 31 s	2 min 05 s
9461259	4	2 min 41 s	4 min 16 s	3 min 00 s	2 min 31s
9635581	4	4 min 58 s	3 min 36 s	3 min 50 s	2 min 32 s
9689788	4	3 min 04 s	2 min 58 s	3 min 07 s	2 min 54 s
	Averaged time	5 min 01 s	3 min 36 s	4 min 05 s	2 min 44 s

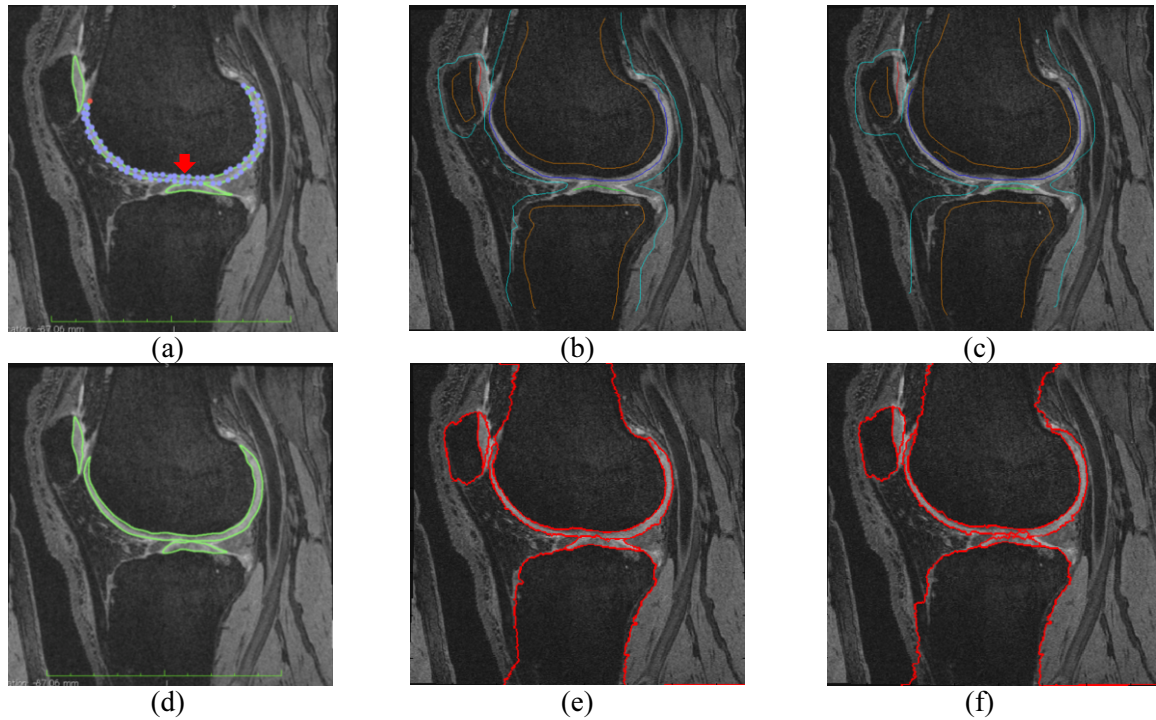


Fig. 5. Comparison between (a) manual segmentation with (b) and (c) interactive segmentations with their results shown in (d), (e) and (f) respectively. Red arrow highlights the region where spline segmentation requires onerous human adjustment.

5. Discussion and conclusion

The objective of this work is to demonstrate the convenience, and test the intuitiveness and efficiency of the proposed software compare to manual segmentation. Open library clinical segmentation software tends to be complicated and used by trained personals and professionals. The proposed software, as shown in Figure 1, is designed to be straightforward and simple. In this software, all buttons are named with common terms like Open, Draw, and Erase and their applications are explicit. Hence, general users can understand the software easily and react accordingly [32]. We noticed that Osirix only offered spline option to delineate the cartilages as shown in Figure 5. Using the proposed software, unique scribbling patterns through the implementation of different functions were exhibited among the users in Table 1 and Figure 5, implying this software was highly adaptive to user intention.

Because various strategies could be developed during scribbling, the recorded computational time and number of clicks vary among different users. While we have developed Erase button for refinement purpose, this function was seldom used by both observers in this study. Instead, we observed that segmentation result produced by random walks algorithm was satisfactory or experienced slight over-segmentation after first round of scribbling. Hence, in most cases, the users have chosen to insert some background seeds near over-segment region to solve this problem. As shown in Table 1, background label has been intensely used by both observers, especially in osteoarthritic images (55 times for observer 1 and 52 times for observer 2).

In Figures 2-5, we have demonstrated that the software functions complement user interaction during seed inserting and result refinement. The Draw button supports dynamic scribbling and therefore,

can support direct human knowledge incorporation. This property suits clinical needs because medical images are usually geometrically complex. In this work, the osteoarthritic cartilage could deform unpredictably [4]. So the users can zoom-in into obscure parts such as patellofemoral sulcus, femorotibial sulcus and other regions with missing boundaries. Table 1 indicates that this function has been used 15 times and 22 times by observer 1 in assessing normal and osteoarthritic images while observer 2 used the function 14 times and 13 times to evaluate normal and osteoarthritic images.

Combined with convenient functions and intuitive software design, the software is able to produce fast 2D segmentation result [33]. According to Tables 2 and 3, the whole procedure after loading the image until final segmentation result display took approximately 2 to 3 minute. The same procedure cost 5 minutes in the case of manual segmentation. The software efficiency is justified in Table 1 where the users achieved final segmentation after running the algorithm approximately 2 times per image. In contrary, manual segmentation was extremely exhaustive and time consuming when dealing with curved knee cartilage. By referring to Figure 5(a), the spline segmentation provided by Orisix was daunting especially when large amounts of control points were squeezed to fit the thin and irregular central femoral cartilage (red arrow). This drawback contributed to longer segmentation duration in both normal and osteoarthritic images. However, we noticed that there was no significant difference in time required to segment osteoarthritic and normal images.

In conclusion, the proposed segmentation software was developed to be user-friendly and efficient for clinical use. Unlike modal based segmentation software, this software is highly adaptive to healthy and osteoarthritic images. Besides, this software is obviously a better alternative to manual segmentation in terms of intuitiveness and efficiency. Nevertheless, this software is far from being accomplished. Future works will extend the applicability of this software to three dimensional (3D) and testing this software using clinical quantitative analysis. Moreover, we suggest seed propagation for subsequent images to accelerate the 3D segmentation procedure after observing the intense use of background seeds in this work.

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References

- [1] F. Eckstein, M. Kunz, M. Schutzer, M. Hudelmaier, R.D. Jackson, J. Yu, C.B. Eaton and E. Schneider, Two year longitudinal change and test-retest-precision of knee cartilage morphology in a pilot study for the osteoarthritis initiative, *Osteoarthritis and Cartilage* **15** (2007), 1326–1332.
- [2] K. Siorpaes, A. Wenger, K. Bloecker, W. Wirth, M. Hudelmaier and F. Eckstein, Interobserver reproducibility of quantitative meniscus analysis using coronal multiplanar DESS and IWTSE MR imaging, *Magnetic Resonance in Medicine* **67** (2012), 1419–1426.
- [3] W. Wirth, M. Nevitt, M.P. Hellio Le Graverand, O. Benichou, D. Dreher, R.Y. Davies, J. Lee, K. Picha, A. Gimona, S. Maschek, M. Hudelmaier and F. Eckstein, Sensitivity to change of cartilage morphometry using coronal FLASH, sagittal DESS, and coronal MPR DESS protocols—comparative data from the osteoarthritis initiative (OAI), *Osteoarthritis and Cartilage* **18** (2010), 547–554.

- [4] H. Shim, S. Chang, C. Tao, J.-H. Wang, C.K. Kwok and K.T. Bae, Knee Cartilage, Efficient and reproducible segmentation on high-spatial-resolution mr images with the semiautomated graph-cut algorithm method1, *Radiology* **251** (2009), 548–556.
- [5] Y. Boykov and M.-P. Jolly, Interactive organ segmentation using graph cuts, in: *Medical Image Computing and Computer-Assisted Intervention – MICCAI*, S. Delp, A. DiGoia and B. Jaramaz, eds., Springer Berlin Heidelberg, 2000, pp. 276–286.
- [6] N. Thi Nhat Anh, C. Jianfei, Z. Juyong and Z. Jianmin, Robust interactive image segmentation using convex active contours, *IEEE Transactions on Image Processing* **21** (2012), 3734–3743.
- [7] Y. Yi, Y. Gao, W. Li and L. Gao, Improved random walker interactive image segmentation algorithm for texture image segmentation, in: *Control and Decision Conference (CCDC)*, 2011, pp. 4163–4166.
- [8] C. Rother, V. Kolmogorov and A. Blake, GrabCut: Interactive foreground extraction using iterated graph cuts, *ACM Trans. Graph.* **23** (2004), 309–314.
- [9] Y.Y. Boykov and M.P. Jolly, Interactive graph cuts for optimal boundary & region segmentation of objects in N-D images, in: *Proceedings of Eighth IEEE International Conference on Computer Vision (ICCV)*, 2001, pp. 105–112.
- [10] L. Grady, Random walks for image segmentation, *IEEE Trans. Pattern Anal. Mach. Intell.* **28** (2006), 1768–1783.
- [11] J. Liu, J. Sun and H.-Y. Shum, Paint selection, in: *ACM SIGGRAPH 2009 papers*, ACM, New Orleans, Louisiana, 2009, pp. 1–7.
- [12] E.N. Mortensen and W.A. Barrett, Interactive segmentation with intelligent scissors, *Graphical Models and Image Processing* **60** (1998), 349–384.
- [13] L. Zhang, H. Kong, C.T. Chin, T. Wang and S. Chen, Cytoplasm segmentation on cervical cell images using graph cut-based approach, *Bio-Medical Materials and Engineering* **24** (2014), 1125–1131.
- [14] H. Su, Z. Su, S. Zheng, H. Yang and S. Wei, Interactive cell segmentation based on phase contrast optics, *Bio-Medical Materials and Engineering* **24** (2014), 29–35.
- [15] J. Folkesson, E. Dam, O. Olsen, P. Pettersen and C. Christiansen, Automatic segmentation of the articular cartilage in knee mri using a hierarchical multi-class classification scheme, in: *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2005*, J. Duncan and G. Gerig, eds., Springer Berlin Heidelberg, 2005, pp. 327–334.
- [16] J.B.D.J. Pang, T.E. McAlindon, J.G. Tamez-Pena, J. Fripp and E.L. Miller, On the use of coupled shape priors for segmentation of magnetic resonance images of the knee, *IEEE Journal of Biomedical and Health Informatics*, 2014. (in press)
- [17] J. B. D. J. Pang, T. E. McAlindon, J. G. Tamez-Pena, J. Fripp and E. L. Miller, “On the use of coupled shape priors for segmentation of magnetic resonance images of the knee,” *IEEE Journal of Biomedical and Health informatics*, 2014. (in press)
- [18] G. Hong-Seng, S. Tan Tian, A.H.A. Karim, K.A. Sayuti, M.R.A. Kadir, T. Weng-Kit, W. Liang-Xuan, K.T. Chaudhary, J. Ali, and P.P. Yupapin, Medical image visual appearance improvement using bihistogram bezier curve contrast enhancement: Data from the osteoarthritis initiative, *The World Scientific Journal* **2014** (2014), 1–13.
- [19] H.-S. G., T.-S. Tan, M.R.B.A. Kadir, A.H.A. Karim, K.A. Sayuti, L.-X. Wong and W.-K. Tham, Medical image contrast enhancement using spline concept: Data from the osteoarthritis initiative, *Journal of Medical Imaging and Health Informatics* **4** (2014), 1–10.
- [20] K.T. Bae, H. Shim, C. Tao, S. Chang, J.H. Wang, R. Boudreau and C.K. Kwok, Intra- and inter-observer reproducibility of volume measurement of knee cartilage segmented from the OAI MR image set using a novel semi-automated segmentation method, *Osteoarthritis and Cartilage* **17** (2009), 1589–1597.
- [21] J. Duryea, G. Neumann, M.H. Brem, W. Koh, F. Noorbakhsh, R.D. Jackson, J. Yu, C.B. Eaton and P. Lang, Novel fast semi-automated software to segment cartilage for knee MR acquisitions, *Osteoarthritis and Cartilage* **15** (2007), 487–492.
- [22] J. Fripp, S. Crozier, S.K. Warfield and S. Ourselin, Automatic segmentation of the bone and extraction of the bone-cartilage interface from magnetic resonance images of the knee, *Physics in Medicine and Biology* **52** (2007), 1617–1631.
- [23] M. Englund, The role of biomechanics in the initiation and progression of OA of the knee, *Best Practice & Research Clinical Rheumatology* **24** (2010), 39–46.
- [24] J.G. Tamez-Pena, J. Farber, P.C. Gonzalez, E. Schreyer, E. Schneider and S. Totterman, Unsupervised segmentation and quantification of anatomical knee features: Data from the osteoarthritis initiative, *IEEE Transactions on Biomedical Engineering* **59** (2012), 1177–1186.
- [25] J. Fripp, S. Crozier, S.K. Warfield and S. Ourselin, Automatic segmentation and quantitative analysis of the articular cartilages from magnetic resonance images of the knee, *IEEE Transactions on Medical Imaging* **29** (2010), 55–64.
- [26] J. Folkesson, E.B. Dam, O.F. Olsen, P.C. Pettersen and C. Christiansen, Segmenting articular cartilage automatically using a voxel classification approach, *IEEE Transactions on Medical Imaging* **26** (2007), 106–115.

- [27] Y. Boykov, O. Veksler and R. Zabih, Fast approximate energy minimization via graph cuts, *IEEE Transactions on Pattern Analysis and Machine Intelligence* **23** (2001), 1222–1239.
- [28] Y. Kang, K. Engelke and W.A. Kalender, Interactive 3D editing tools for image segmentation, *Medical Image Analysis* **8** (2004), 35–46.
- [29] L. Grady, Multilabel random walker image segmentation using prior models, in: *IEEE Computer Society Conference on Computer Vision and Pattern Recognition (CVPR)*, 2005, 763–770.
- [30] F. Eckstein, M. Hudelmaier, W. Wirth, B. Kiefer, R. Jackson, J. Yu, C.B. Eaton and E. Schneider, Double echo steady state magnetic resonance imaging of knee articular cartilage at 3 Tesla: A pilot study for the osteoarthritis initiative, *Annals of the Rheumatic Diseases* **65** (2006), 433–441.
- [31] C.G. Peterfy, E. Schneider and M. Nevitt, The osteoarthritis initiative: Report on the design rationale for the magnetic resonance imaging protocol for the knee, *Osteoarthritis and Cartilage* **16** (2008), 1433–1441.
- [32] S. Olabariaga and A.M. Smeulders, Setting the mind for intelligent interactive segmentation: Overview, requirements, and framework, in: *Information Processing in Medical Imaging*, J. Duncan and G. Gindi, eds., Springer Berlin Heidelberg, 1997, pp. 417–422.
- [33] J. Pang, J. Drihan, G. Destenaves, E. Miller, G. Lo, R. Ward, L.L. Price, J. Lynch, C. Eaton, F. Eckstein and T. McAlindon, Quantification of bone marrow lesion volume and volume change using semi-automated segmentation: Data from the osteoarthritis initiative, *BMC Musculoskeletal Disorders* **14** (2013), 1–19.