Proceedings of NFSI & ICFBI 2007
Hangzhou, China, October 12-14, 2007

Medical Image Segmentation: Methods and Software

D.J. Withey and Z.J. Koles[1, 2]
[1]Department of Electrical and Computer Engineering, [2]Department of Biomedical Engineering,
University of Alberta, Edmonton, Alberta, CANADA
dwithey@ece.ualberta.ca, z.koles@ualberta.ca

Abstract-**Methods for segmentation of medical images are divided into three generations, where each generation adds an additional level of algorithmic complexity. The first generation is composed of the simplest forms of image analysis such as the use of intensity thresholds and region growing. The second generation is characterized by the application of uncertainty models and optimization methods, and the third generation incorporates knowledge into the segmentation process. Sources of segmentation software from industry and academia are identified along with databases for segmentation validation.**

I. Introduction

Segmentation is the process of dividing images into constituent subregions. Manual segmentation is possible but is a time-consuming task and subject to operator variability. Reproducing a manual segmentation result is difficult and the level of confidence ascribed suffers accordingly. Automatic methods are, therefore, preferable [1]; however, significant problems must be overcome to achieve segmentation by automatic means and it remains an active research area [1]-[5].

Segmentation of medical images involves three main image-related problems. Images contain *noise* that can alter the intensity of a pixel such that its classification becomes uncertain, images exhibit *intensity nonuniformity* where the intensity level of a single tissue class varies gradually over the extent of the image, and images have finite pixel size and are subject to *partial volume averaging* where individual pixel volumes contain a mixture of tissue classes so that the intensity of a pixel in the image may not be consistent with any one class.

These problems and the variability in tissue distribution among individuals in the human population means that some degree of uncertainty must be attached to all segmentation results. This includes segmentations performed by medical experts where variability occurs between experts (inter-observer variability) as well as for a given expert performing the same segmentation on multiple occasions (intra-observer variability). Despite this variability, image interpretation by medical experts is generally considered to be the only available truth for in vivo imaging [1].

We classify the medical image segmentation literature into three generations, each representing a new level of algorithmic development. The earliest and lowest-level processing methods occupy the first generation. The second is composed of algorithms using image models, optimization methods, and uncertainty models, and the third is characterized by algorithms that are capable of incorporating knowledge. These generations indicate progress towards fully-automatic medical image segmentation and their identification provides a framework for classifying the wide variety of methods that have been devised.

We focus primarily on the segmentation of magnetic resonance (MR) head images although many methods can also be applied to other image types and to images from other modalities.

Automatic segmentation methods have been previously classified as either supervised or unsupervised [2]. Supervised segmentation requires operator interaction throughout the segmentation process whereas unsupervised methods generally require operator involvement only after the segmentation is complete. Unsupervised methods are preferred to ensure a reproducible result [1]; however, operator interaction is still required for error correction in the event of an inadequate result [3].

In the following, the three generations of medical image segmentation are first identified along with a representative set of examples for each and a summary in figure 1. Descriptions of available segmentation software and of on-line, image databases with ground-truth segmentations suitable for algorithm evaluation are also provided.

II. First Generation

The first-generation includes low-level techniques where little, if any, prior information is included. They are subject to all three of the main image segmentation problems. Further description can be found in textbooks on image processing, e.g. [6], [7].

Thresholds: Applied to an image to distinguish regions with contrasting intensity levels.

Region Growing: Beginning at a seed location in the image, adjacent pixels are checked against a predefined homogeneity criterion. Pixels that meet the criterion are included in the region. Continuous application of this rule allows the region to grow, defining the volume of an object in the image by identification of similar, connected pixels.

Edge Tracing: Edge detection forms an edge image after which edge pixels with adjacent neighbor connectivity are followed sequentially and collected into a list to represent an object boundary [6]. The search for neighboring pixels is heuristic in nature.

III. Second Generation

Research in automatic image segmentation diverges from the first-generation algorithms with the introduction of uncertainty models and optimization methods as well as a general avoidance of heuristics. Efforts are made to overcome the three

1-4244-0949-7/07/$25.00

main segmentation problems but segmentation results remain data-dependent.

Statistical Pattern Recognition: A mixture model is used where each of the pixels in an image is modeled as belonging to one of a known set of classes. Bayesian classifiers, discriminant analysis, and k-Nearest Neighbor classification are examples of supervised methods [8]. Unsupervised, statistical clustering using expectation-maximization (EM) has allowed segmentation and nonuniformity gain field estimation to occur simultaneously [9]. Contextual information has been included using a Markov random field (MRF) and hidden MRF [10], reducing misclassification.

C-means Clustering: Image pixels are grouped together based on a set of descriptive features [2]. The numerical value of each feature is generally normalized to between 0 and 1 and the number of clusters is assumed to be known. Iterative algorithm execution is terminated when the first local minimum is reached. Fuzzy c-means clustering (FCM), for example, has been applied to medical images [4].

Deformable Models: These are artificial, closed contours/surfaces able to expand or contract over time, within an image, and conform to specific image features. Active contours and active surfaces are included in this category. Energy-minimization models [11] and front-propagation methods based on level-sets [12] are common types. Propagation is toward a local optimum.

Graph Search: Image pixels are used to form nodes in a graph and the nodes are interconnected to neighbors, mapping the corresponding pixel associations in the image. Costs are assigned for each interconnection. Algorithms from combinatorial optimization are used to obtain minimum-cost solutions.

A graph cut is a set of interconnections between nodes in a graph which, when removed, partition the graph into two distinct sets. Graph cuts are related to active contours and level-sets which are their continuous-space analogs [13].

Fuzzy Connectedness [14] and the Watershed Algorithm [15] are examples of graph-search algorithms used in medical image segmentation. A generalization unifying all optimal, graph-search algorithms is provided in [16].

Neural Networks: Many neural networks must first be trained with suitable image data, after which they can be used to segment other images [2]. It has been noted that neural network models often have an implicit equivalence to a corresponding statistical pattern recognition method [17]. Specific, biological models are used in some types [18].

Neuro-fuzzy systems, combinations of neural networks and fuzzy systems, have also been used in image segmentation. A brief survey can be found in [19].

Multiresolution Methods: Multiresolution, multiscale, and pyramid analysis refer to the use of scale reduction to group pixels into image objects. A stack of images is formed by recursively reducing the scale of the original image by blurring followed by down sampling. Pixels are linked from one layer in the stack to the next using similarity attributes [20]. Boundaries have also been refined using a multiscale approach [21].

Minimal Path: Edge following has been performed by computing geodesic contours, as used in deformable models based on the methods of level sets [22].

Target Tracking: Automatic, target-tracking algorithms employing the discrete Kalman filter have also been used for edge following [23], [24].

IV. Third Generation

While second-generation optimization methods and uncertainty models are important and should be used, they are not sufficient in themselves to produce accurate, automatic segmentations, in the general case. Methods that incorporate higher-level knowledge such as a priori information, expert-defined rules, and models (e.g. shape) of a desired object constitute the third generation.

Shape Models: The active shape model (ASM) [25] was inspired by deformable models with the added intention of limiting the extent of the model deformation. A statistical representation of an object is formed by identifying a set of landmark points on an object boundary and analyzing the variation of each across a set of training images. The ASM is then used to identify objects of the same class within other images. Deformation occurs as with deformable models but is restricted to within the bounds of the statistical model.

Related shape-based approaches to image segmentation have also been developed, e.g. [26], and other shape representations, e.g. [27], have also been used. A level-set shape representation that permits surface topology modification as the model deforms has also been introduced [28].

Appearance Models: An active appearance model (AAM) is an extension of an ASM where shape plus intensity of an object, referred to as an image patch, are integrated into a statistical model [29]. A brief survey describing a number of AAM variants can be found in [30].

Atlas-based Segmentation: An atlas is a composite image formed from segmented, co-registered images of several subjects. A 3D mapping is determined between the atlas and an image with unknown segmentation and the atlas supplies prior probabilities for statistical pattern recognition, e.g. [31].

In many cases, the use of an atlas requires distinct steps for registration and for segmentation. A method for jointly performing these steps has been reported [32].

Although fully-automatic registration is desirable, semiautomatic registration is also used where manually-defined, landmark points constrain the deformation and improve segmentation accuracy especially in cortical regions where substantial inter-subject variability exists [33].

Many atlases contain probabilistic information but fuzzy templates have also been formed [34].

Rule-based Segmentation: Automatic, rule-based guidance of unsupervised image segmentation has been explored in an attempt to improve the results from unsupervised segmentation methods and yet maintain an automated approach to the segmentation task. Image primitives are usually derived from first-generation and second-generation algorithms and then interpreted using anatomical and image knowledge applied as a set of rules.

A wide variety of methods have been developed. Examples are: possibilistic clustering and fuzzy logic with human-expert linguistic descriptions of object position and features [35]; and, simultaneous deformation of a set of mesh surfaces, guided by medical knowledge of the shape and texture of the objects of interest, applied as a series of rules [36].

Coupled Surfaces: Segmentation using deformable models [37] and graph-cut methods [38] has been improved by simultaneously identifying multiple surfaces and requiring that a known spatial relationship be maintained.

V. Segmentation Software

A sampling of software from commercial, government, and research sources is given in this section. A larger list is maintained in the Internet Analysis Tools Registry [39] by the Center for Morphometric Analysis (CMA) at the Massachusetts General Hospital (MGH), an affiliate of Harvard University. Also, the Neuro Image Analysis group at the University of North Carolina maintains a webpage with links to software-download sites [40].

BIC Software Toolbox: The McConnell Brain Imaging Centre (BIC) of the Montreal Neurological Institute (MNI) at McGill University freely offers a variety of software for medical image analysis [41]. Included are tools for automatic registration, segmentation, intensity nonuniformity correction, sulcus extraction and labeling, and cortex extraction. Tools for PET and fMRI analysis are also available.

SPM: Statistical Parametric Mapping (SPM) developed at the Wellcome Department of Cognitive Neurology, University College of London, England, is freely available software intended for analysis of brain imaging data sequences [42]. Supported modalities include fMRI, PET, SPECT, EEG and MEG. Segmentation in SPM is performed using unsupervised, statistical clustering.

FSL: The FMRIB Software Library (FSL) was developed by the Oxford Center for Functional Magnetic Resonance Imaging of the Brain (FMRIB) at the University of Oxford, England. It contains image analysis tools for fMRI, structural MRI, and diffusion tensor imaging data. Segmentation of head images is performed by application of an automated, brain extraction tool based on a deformable model, followed by automatic segmentation of gray matter, white matter, and cerebrospinal fluid using the method of [10]. The FSL software is freely available for noncommercial use [43].

MEDx: A commercial software package developed by Sensor Systems Medical Products Division [44] located in Sterling, Virginia, USA. Both SPM and FSL are used in MEDx.

EIKONA3D: A commercial software package developed by Alpha Tec, Ltd. [45], located in Thessaloniki, Greece. Interactive image segmentation can be performed by threshold and by region-based methods, such as region growing. Basic edge detection and edge-following features are also available.

FreeSurfer: FreeSurfer [46] is a software package developed by CorTechs Labs [47] and the Athinoula A. Martinos Center for Biomedical Imaging [48] at MGH. The software employs automatic and manual segmentation methods for reconstruction of the cerebral cortex from structural, MR images and also allows overlay of fMRI and EEG data onto the reconstructed surface.

Insight Segmentation and Registration Toolkit (ITK): This toolkit [49] and its companion the visualization toolkit (VTK) [50] have been developed by the United States National Library of Medicine in support of the Visible Human Project. Development began in 1999 and is ongoing. The toolkits are open-source, freely available, software modules written in C++ (with Tcl/Java/Python bindings) and supported by Kitware [51]. The modules are building blocks for image segmentation and registration software applications.

The segmentation modules include a variety of low-level methods as well as higher-level segmentation using, for example, the watershed algorithm and deformable models.

Analyze: A commercial, image analysis, software package developed by the Biomedical Imaging Resource at the Mayo Foundation [52] based in Rochester, Minnesota, USA. The software permits automatic segmentation using modules from ITK, including segmentation based on level-sets, fuzzy connectedness, and the watershed algorithm. A number of lower-level filtering functions are also available.

3D Slicer: Developed by the MIT Artificial Intelligence Lab and the Surgical Planning Lab at Brigham and Women's Hospital, an affiliate of Harvard Medical School, 3DSlicer is open-source, freely-available software based on VTK and ITK. Segmentation is performed via manual and semiautomatic means. A module that performs pixel classification using the EM algorithm is also included [53].

VI. Validation Databases

Evaluation of results from automatic segmentation of in vivo images is usually accomplished by comparison with segmentations formed by experts. Additional evaluation of an algorithm is possible by the analysis of synthetic images or images of physical phantoms [4].

MNI: The McConnell Brain Imaging Centre of the MNI has developed a synthetic brain database using MR simulation [54]. A range of noise and intensity nonuniformity can be obtained.

IBSR: The Internet Brain Segmentation Repository (IBSR) [55], operated by CMA at MGH, contains MR images with manually-guided segmentations. Head images of more than 40 subjects are available. In some, up to 43 individual structures have been manually identified.

SBIA: The Section for Biomedical Image Analysis (SBIA) in the department of Radiology at the University of Pennsylvania [56] has software for generating simulated inter-subject head deformations. This is intended for validation studies of atlas-based segmentation methods.

Generation	Category		
	Region-based	**Boundary Following**	**Pixel Classification**
1st	• Region growing	• Edge tracing (heuristic)	• Intensity threshold
2nd	• Deformable models • Graph search	• Minimal path • Target tracking • Graph search • Neural networks • Multiresolution	• Statistical pattern recognition • C-means clustering • Neural networks • Multiresolution
3rd	• Shape models • Appearance models • Rule-based • Coupled surfaces		• Atlas • Rule-based

Fig. 1. Method Summary

REFERENCES

[1] L.P. Clarke, R.P. Velthuizen, M.A. Camacho, J.J. Heine, M. Vaidyanathan, L.O. Hall, R.W. Thatcher, M.L. Silbiger, "MRI segmentation: Methods and applications," *Magn. Reson. Imaging*, vol. 13, no. 3, pp. 343-368, 1995.

[2] J.C. Bezdek, L.O. Hall, L.P. Clarke, "Review of MR image segmentation techniques using pattern recognition," *Med. Phys.,* vol. 20, no. 4, pp. 1033-1048, 1993.

[3] S.D. Olabarriaga, A.W.M. Smeulders, "Interaction in the segmentation of medical images: A survey," *Med. Image Anal.*, vol. 5, pp. 127-142, 2001.

[4] D.L. Pham, C. Xu, J.L. Prince, "Current methods in medical image segmentation," *Annu. Rev. Biomed. Eng.*, vol. 2, pp. 315-337, 2000.

[5] J.S. Duncan, N. Ayache, "Medical image analysis: Progress over two decades and the challenges ahead," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 22, no. 1, pp. 85-106, 2000.

[6] I. Pitas, "Digital Image Processing Algorithms," Prentice-Hall, 1993.

[7] W.K. Pratt, "Digital Image Processing," John Wiley & Sons, Inc., 1991.

[8] P. Anbeek, K.L. Vincken, G.S. van Bochove, M.J.P. van Osch, J. van der Grond, "Probabilistic segmentation of brain tissue in MR imaging," *NeuroImage*, vol. 27, pp. 795-804, 2005.

[9] W.M. Wells III, W.E.L. Grimson, R. Kikinis, F.A. Jolesz, "Adaptive segmentation of MRI data," *IEEE Trans. Med. Imag.*, vol. 15, no. 4, pp. 429-442, 1996.

[10] Y. Zhang, M. Brady, S. Smith, "Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm," *IEEE Trans. Med. Imag.*, vol. 20, no. 1, pp. 45-57, 2001.

[11] T. McInerney, D. Terzopoulos, "Deformable models in medical image analysis: A survey," *Med. Image Anal.*, vol. 1, no. 2, pp. 91-108, 1996.

[12] J.A. Sethian, "Level set methods and fast marching methods," Cambridge University Press, 1999.

[13] Y. Boykov, G. Funka-Lea, "Graph cuts and efficient N-D image segmentation," *Int. J. Comput. Vision*, vol. 70, no. 2, pp. 109-131, 2006.

[14] J.K. Udupa, P.K. Saha, "Fuzzy connectedness and image segmentation," *Proceedings of the IEEE,* vol. 91, no. 10, pp. 1649-1669, 2003.

[15] L. Vincent, P. Soille, Watersheds in digital spaces: An efficient algorithm based on immersion simulations, *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 13, no. 6, pp. 583-598, 1991.

[16] A.X. Falcão, J. Stolfi, R. de Alencar Lotufo, "The image foresting transform: Theory, algorithms, and applications," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 26, no. 1, pp. 19-29, 2004.

[17] A.K. Jain, R.P.W. Duin, J. Mao, "Statistical pattern recognition: A review," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 22, no. 1, pp. 4-37, 2000.

[18] J.L. Johnson, M.L. Padgett, "PCNN models and applications," *IEEE Trans. Neural Networks*, vol. 10, no. 3, pp. 480-498, 1999.

[19] V. Boskovitz, H. Guterman, "An adaptive neuro-fuzzy system for automatic image segmentation and edge detection," *IEEE Trans. Fuzzy Systems*, vol. 10, no. 2, pp. 247-262, 2002.

[20] W.J. Neissen, K.L Vinken, J. Weickert, B.M. Ter Haar Romeny, M.A. Viergever, "Multiscale segmentation of three-dimensional MR brain images," *Int. J. Comput. Vision*, vol. 31, pp. 185-202, 1999.

[21] S.V. Raman, S. Sarkar, K.L. Boyer, "Tissue boundary refinement in magnetic resonance images using contour-based scale space matching," *IEEE Trans. Med. Imag.*, vol. 10, no. 2, pp. 109-121, 1991.

[22] L.D. Cohen, R. Kimmel, "Global minimum for active contour models: A minimal path approach," *Int. J. Comput. Vision*, vol. 24, no. 1, pp. 57-78, 1997.

[23] P. Abolmaesumi, M.R. Sirouspour, "An interacting multiple model probabilistic data association filter for cavity boundary extraction from ultrasound images," *IEEE Trans. Med. Imag.*, vol. 23, no. 6, pp. 772-784, 2004.

[24] D. Withey, "Dynamic Edge Tracing: Recursive methods for medical image segmentation," Ph.D. dissertation, University of Alberta, Edmonton, Alberta, Canada, 2006.

[25] T.F. Cootes, C.J. Taylor, D.H. Cooper, J. Graham, "Active shape models – Their training and application," *Comput. Vis. Image Understanding*, vol. 61, no. 1, pp. 38-59, 1995.

[26] C. Davatzikos, X. Tao, D. Shen, "Hierarchical active shape models, using the wavelet transform," *IEEE Trans. Med. Imag.*, vol. 22, no. 3, pp. 414-423, 2003.

[27] S.M. Pizer, P.T. Fletcher, S. Joshi, A. Thall, J.Z. Chen, Y. Fridman, D.S. Fritsch, A.G. Gash, J.M. Glotzer, M.R. Jiroutek, C. Lu, K.E. Muller, G. Tracton, P. Yushkevich, E.L. Chaney, "Deformable M-reps for 3D medical image segmentation," *Int. J. Comput. Vision*, vol. 55, pp. 85-106, 2003.

[28] M.E. Leventon, W.E.L. Grimson, O. Faugeras, "Statistical shape influence in geodesic active contours," in: IEEE Conference on Computer Vision and Pattern Recognition, vol. 1, pp. 316-323, 2000.

[29] T.F. Cootes, G.J. Edwards, C.J. Taylor, "Active appearance models," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 23, no. 6, pp. 681-685, 2001.

[30] R. Beichel, H. Bischof, F. Leberl, M. Sonka, "Robust active appearance models and their application to medical image analysis," *IEEE Trans. Med. Imag.*, vol. 24, no. 9, pp. 1151-1169, 2005.

[31] C.A. Cocosco, A.P. Zijdenbos, A.C. Evans, "A fully automatic and robust brain MRI tissue classification method," *Med. Image Anal.*, vol. 7, pp. 513-527, 2003.

[32] K.M. Pohl, J. Fisher, W.E.L. Grimson, R. Kikinis, W.M. Wells, "A Bayesian model for joint segmentation and registration," *NeuroImage*, vol. 31, pp. 228-239, 2006.

[33] L.A. Dade, F.Q. Gao, N. Kovacevic, P. Roy, C. Rockel, C.M. O'Toole, N.J. Lobaugh, A. Feinstein, B. Levine, S.E. Black, "Semiautomatic brain region extraction: A method of parcellating brain regions from structural magnetic resonance images," *NeuroImage*, vol. 22, pp. 1492-1502, 2004.

[34] J. Zhou, J.C. Rajapakse, "Segmentation of subcortical brain structures using fuzzy templates," *NeuroImage*, vol. 28, pp. 915-924, 2005.

[35] V. Barra, J.-Y. Boire, "Automatic segmentation of subcortical brain structures in MR images using information fusion," *IEEE Trans. Med. Imag.*, vol. 20, no. 7, pp. 549-558, 2001.

[36] A. Pitiot, H. Delingette, P.M. Thompson, N. Ayache, "Expert knowledge-guided segmentation system for brain MRI," *NeuroImage*, vol. 23, pp. S85-S96, 2004.

[37] X. Zeng, L.H. Staib, R.T. Schultz, J.S. Duncan, "Segmentation and measurement of the cortex from 3-D MR images using coupled-surfaces propagation," *IEEE Trans. Med. Imag.*, vol. 18, no. 10, pp. 927-937, 1999.

[38] K. Li, X. Wu, D.Z. Chen, M. Sonka, "Optimal surface segmentation in volumetric images – A graph theoretic approach," *IEEE Trans. Pattern Anal. Mach. Intell.*, vol. 28, no. 1, pp. 119-134, 2006.

[39] http://www.cma.mgh.harvard.edu/iatr/

[40] http://www.ia.unc.edu/dev/download/

[41] http://www.bic.mni.mcgill.ca/software/

[42] http://www.fil.ion.ucl.ac.uk/spm/

[43] http://www.fmrib.ox.ac.uk/fsl/

[44] http://medx.sensor.com/products/medx/overview.html

[45] http://www.alphatecltd.com/eikona3d/imageprocessing3d.html

[46] http://surfer.nmr.mgh.harvard.edu

[47] http://www.cortechs.net/

[48] http://www.nmr.mgh.harvard.edu/martinos/flashHome.php

[49] http://www.itk.org

[50] http://public.kitware.com/VTK/

[51] http://www.kitware.com

[52] http://www.mayo.edu/bir/Software/Analyze/Analyze.html

[53] http://www.slicer.org/

[54] http://www.bic.mni.mcgill.ca/brainweb/

[55] http://www.cma.mgh.harvard.edu/ibsr/

[56] http://www.rad.upenn.edu/sbia/