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Optimization-Based Interactive Segmentation Interface for Multi-Region Problems

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Abstract. Interactive segmentation is becoming of increasing interest to the medical imaging community in that it combines the positive aspects of both manual and automated segmentation. However, general purpose tools have been lacking in terms of segmenting multiple regions simultaneously with a high degree of coupling between groups of labels. Hierarchical max-flow segmentation has taken advantage of this coupling for individual applications, but until recently these algorithms were constrained to a particular hierarchy and could not be considered general-purpose. In a generalized form, the hierarchy for any given segmentation problem is specified in run-time, allowing different hierarchies to be quickly explored. This paper presents a novel interactive segmentation interface, which uses generalized hierarchical max-flow for optimization-based multi-region segmentation guided by user-defined seeds. Applications in cardiac and neonatal brain segmentation are given as example applications of its generality.

Keywords: hierarchical max-flow segmentation, interactive segmentation, optimization-based segmentation, convex optimization, ASETS library.

1 Introduction

Interactive segmentation is the middle-ground between fully manual segmentation, where a user manually contours slices of a 3D medical image to define objects of interest, and automated segmentation where, with minimal user input, an algorithm attempts the segmentation task with no guidance or interaction with the user. The former is widely known to be time consuming, and subject to inadequacies regarding the number of slices segmented and the consistency between segmentations. The latter is often very rigid, being specific to particular anatomy of interest in a designated modality under specific conditions, and difficult to incorporate anatomical knowledge into especially in the presence of pathology. In interactive segmentation, the user and algorithm work together, with the user providing initial input and corrections, while the algorithm ensures the consistency of the segmentation across slices.¹ Interactive segmentation has long been known to improve segmentation time and consistency for tasks in which manual segmentation would otherwise be necessary.²

From a purely input-output point of view, interactive segmentation programs only differ in terms of the mechanisms in which the user can provide information, and the algorithms used to process said information. More specifically, interactive segmentation programs differ in terms of:

- the number of labels allowed by the interface and their topology (label orderings),
- the sampling mechanisms available to the user such as paint-brushes, contours, etc... ,
- the algorithms which process this sampled data to derive a labeling, and
- the organization of the multiple processing components used which together form the segmentation pipeline.

These variables are inter-related, with the number of labels and types of sampling mechanisms constraining the types of algorithms available, and the types of algorithms constrain what types of algorithm organizations are meaningful. These factors dictate the scope of segmentation problems that can be readily addressed.

The number of labels allowed by the interactive segmentation interface is arguably the simplest method for categorizing interactive segmentation interfaces. Early methods in interactive segmentation, such as Interactive graph-cuts,³ Grab-cut,⁴ and Intelligent Scissors⁵ were constrained to the use of only two labels: foreground and background. TurtleSeg^{6,7} and ITK-Snap⁸ permit the use of an arbitrary number of labels, making them better suited for multi-region problems. As of yet, there are no prior interactive segmentation that consider label orderings as a form of input. However, several take advantage of a particular label ordering suited to a particular segmentation problem.^{9,10}

In terms of sampling image data to build a descriptive data model, interactive graph-cuts³ used a paint-brush mechanism, Intelligent Scissors⁵ and TurtleSeg^{6,7} a contouring mechanism, and ITK-Snap⁸ provides mechanisms for both. Some interactive segmentation frameworks, such as the MIDAS framework,¹¹ provide limited direct user manipulation of labels, shifting its focus to the user definition of pipelines containing fundamental segmentation algorithms, such as thresholding and region growing, and morphological operators with an emphasis on segmentation reproducibility.

Interactive segmentation interfaces display a considerable amount of variability in terms of the algorithms available to extrapolate the user’s sampling information and other indications. Several methods utilize optimization based approaches ranging from shortest path algorithms⁵ to discrete graph cuts,^{3,4} level-sets,⁸ and random walk based segmentation.^{6,7,12} These algorithms generally have a fairly rigid organization, with the exception of interfaces in which pipelines are the primary focus of user interaction.¹¹

As stated earlier, one issue with general-purpose interactive segmentation programs is their overall lack of explicit incorporation of anatomical knowledge in an intuitive manner. Initially, the concept of incorporating anatomical knowledge into a general-purpose (and therefore application/modality agnostic) program may seem paradoxical. However, certain abstract forms of anatomical knowledge about the spatial arrangement between objects may be expressed quickly and easily while maintaining generality across algorithms. The application of hierarchies to segmentation and natural scene understanding has been well-studied,^{13,14} but often treats the hierarchy as a structure that the algorithm must learn aside from user input.

In this work, we allow the user to explicitly define a segmentation hierarchy which can be optimized globally using generalized hierarchical max-flow (HMF).^{15,16} These hierarchies express object grouping behaviour by way of partitioning. For example, one can think of a super-object, such as the heart, as being comprised of several sub-objects (the left and right ventricles and atria) with can be recursively sub-divided (blood pool and wall). These partitioning relationships allows for nuanced regularization requirements to be described.

2 Methods

2.1 Hierarchical max-flow segmentation

Hierarchical max-flow (HMF) models^{15,16} extend the notion of orderings from the Ishikawa model^{17,18} to hierarchies. In this case, collections of labels can be unioned to create a super-label. This process repeats itself until the entire image is represented as a single label, denoted as S or the root

label. (Such S labels are shown at the top of the hierarchies in Figures 5 and 6.) Alternatively, one can take a top-down interpretation, recursively splitting objects in the image into their constituent parts. The formula for these models is:

$$\begin{aligned}
& \min_u \sum_{\forall L \in \mathbb{L}} \int_{\Omega} D_L(x) u_L(x) dx + \sum_{\forall L \in \mathbb{G}} \int_{\Omega} S_L(x) |\nabla u_L(x)| dx \\
& \text{s.t. } \forall L \in \mathbb{L}, (u_L(x) \geq 0), \sum_{\forall L \in \mathbb{L}} u_L(x) = 1 \\
& \forall L \in \mathbb{G}, \left(\sum_{L' \in L.C} u_{L'}(x) = u_L(x) \right)
\end{aligned} \tag{1}$$

The operator $.C$ refer to parent/child relationships in the hierarchy, specifically, $L.C$ returns the set of child labels of label L . This formula is similar to that of the continuous Potts model¹⁹ in that it contains a series of unary data terms, $D_L(x)$, and a set of regularization or weighting terms, $S_L(x)$, on the gradient magnitude of each labeling function, $|\nabla u_L(x)|$, and that these terms are summed over each label (and super-label). These hierarchical models are strictly more expressive than both Potts²⁰ and Ishikawa¹⁷ models together,¹⁵ allowing for a wider array of segmentation problems to be addressed. However, hierarchies are more difficult to specify.

This tree structure has previously been considered a hard-coded part of the image segmentation algorithm, encouraging the use of Potts²⁰ or Ishikawa¹⁷ models and their continuous max-flow counterparts^{18,19} to handle general-purpose segmentation. However, this poses fundamental limitations on what can be segmented. For example, in the Potts model, only a single smoothness parameter is assigned, which makes it difficult to simultaneously segment smooth structures alongside irregular ones. Ishikawa models allow for more parameterization, but require the objects being segmented to satisfy a full ordering, which is not the case for complex anatomy.

The general HMF solver alleviates this problem by permitting any arbitrary hierarchy to be defined, allowing for more anatomical knowledge to be encoded. This intuitive form of anatomic knowledge can be readily incorporated into the optimization-based segmentation of multiple regions. Problems regarding constructing the largest meaningful hierarchy given label grouping information are NP-hard (See Appendix), meaning that interactive methods, at least for hierarchy definition may be required so as to make use of a user’s anatomical knowledge.

Details of the precise implementation of the HMF solver can be found in the technical report.¹⁵ The solver is provided open-source at <http://www.advancedsegmentationtools.org/> in both MATLAB and C++ implementations.

2.2 Definition of Cost Terms

A crucial decision in optimization-based segmentation is the structure of the cost terms. Log-likelihood data terms, derived from Bayes’ theorem, have been effective in interactive³ and multi-region segmentation,²¹ taking the form:

$$D_L(x) = \begin{cases} \infty, & \text{if } x \text{ is a seed for a label other than } L \text{ or element of } L.P^* \\ -\ln(P(I(x)|x \in L)), & \text{else} \end{cases} \tag{2}$$

where $P(I(x)|x \in L)$ is the likelihood of a voxel in label L having the same intensity as x , $I(x)$ and $L.P^*$ is the set of ancestors (parents, grandparents, etc...) of label L . The probability, $P(I(x)|x \in L)$, is estimated from the histogram of the seeded voxels, which approximates the true value when a large number of seeds is used. The infinite cost ensures that any voxels used to seed a particular object remain a part of said object in the segmentation and that any voxel which has been seeded as a particular label can only be assigned to said label if it is an end-label or to its child labels otherwise.

Smoothness or regularization terms are non-negative costs used to both smooth the labeling and to align edges in the segmentation with those visible in the underlying image. The smoothness terms used were:

$$S_L(x) = \alpha_L * \exp(-\beta_L |\nabla I(x)|) + \gamma_L, \quad (3)$$

where the parameters α_L , β_L , and γ_L are specified by the user. The exponential term implies that lower costs are associated with label boundaries which occur when there is a high gradient magnitude, encouraging nearby edges in the segmentation to migrate to said areas similar to the contrast sensitive smoothness terms used by Boykov *et al.*³

2.3 Plane Selection

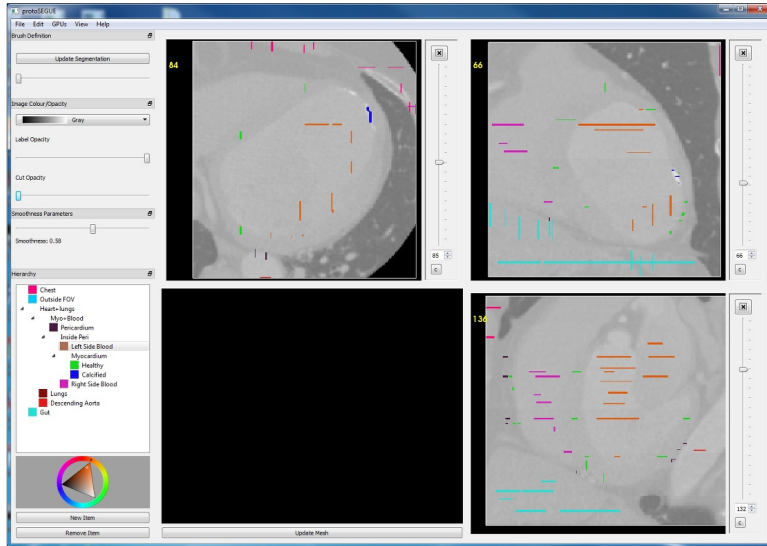
To improve efficiency and accuracy while encouraging interactivity, plane selection can be used.⁶ Such planes can be used by the algorithm to inform the user as to which areas of the segmentation would benefit the most from user interaction. Top *et al.*⁶ introduced a notion of active learning in which the segmentation algorithm identifies areas of maximum uncertainty, the uncertainty of a segmentation expressed as:

$$U(x, y) = \lambda_E U_E(x, y) + \lambda_B U_B(x, y) + \lambda_R U_R(x, y) + \lambda_S U_S(x, y) \quad (4)$$

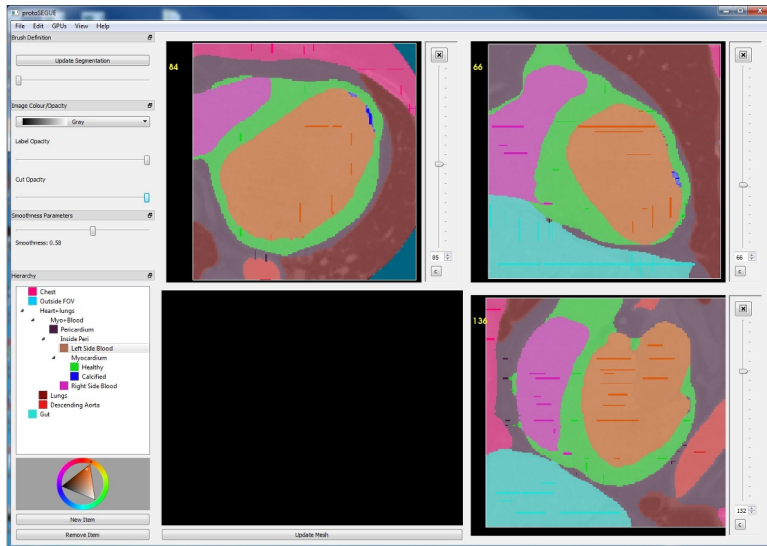
where U_E is the entropy of the segmentation results, U_B the uncertainty associated with boundaries in the segmentation, U_R the the uncertainty associated with the regional intensity, and U_S the uncertainty associated with the tortuosity of the boundary around x . The λ 's are constants with the majority (80%) of the weight given to λ_E .⁶ Note that the U_R and U_B terms are explicitly handled by the segmentation algorithm itself by the definition of the cost functions. We assign all the weight to the U_E term and use only maximum axis-aligned planes. This ensures that the plane selection algorithm quickly produces planes in orientations to which the user is accustomed. The segmentation used in plane selection is the previous segmentation generated by the user. Thus, plane selection is only defined after the first segmentation is computed and remains available for all subsequent interactions.

3 Interface Description

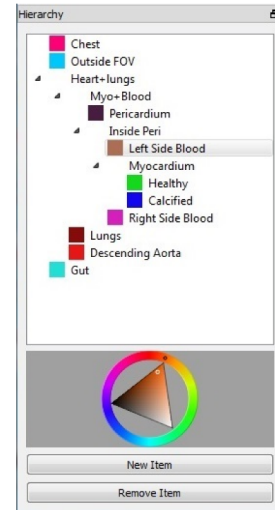
The interface is implemented using Kitware's Visualization Tool-Kit (VTK) for image processing and visualization and the Qt framework for graphical user interface support. The generalized HMF solver was encapsulated into a VTK algorithm object and accelerated using NVIDIA's Compute Unified Device Architecture (CUDA). The sampling mechanism is brush-based similar to that used by Boykov *et al.*³ and ITK-Snap⁸ allowing for large portions of an object's interior to be covered



(a) Interface with seeding



(b) Interface after labeling is performed with provided seeds



(c) Widget for hierarchy definition

Fig 1: Segmentation interface with user seeds before segmentation (a) and after segmentation (b). The hierarchy definition widget (bottom left corner of (a) and (b)) is shown enlarged in (c).

with relative ease while not requiring strong boundary contrast. The user can place seeds for any label or super-label using the brush, creating the data model described in Eq. (2).

The interface is shown in Figure 1. Hierarchies are defined in a side bar as shown in Figure 1(c), which also acts as a widget for selecting the active label or super-label of the brush. This widget also allows the hierarchy to be restructured quickly, operating in a drag-and-drop manner. Lastly, the user can save the hierarchy along with smoothness term parameters and the initial user-defined samples for later use.

4 Example Applications of Interactive Segmentation

4.1 Cardiac Segmentation

Because of the generality of the algorithm and the interface, several existing continuous max-flow based methods, such as those developed by Rajchl *et al.*,^{9,10} can be easily replicated. We reproduced the experiments performed in,⁹ which included 3 cardiac volumes from computed tomography (CT), magnetic resonance angiography (MRA), and trans-esophageal echocardiography (TEE).

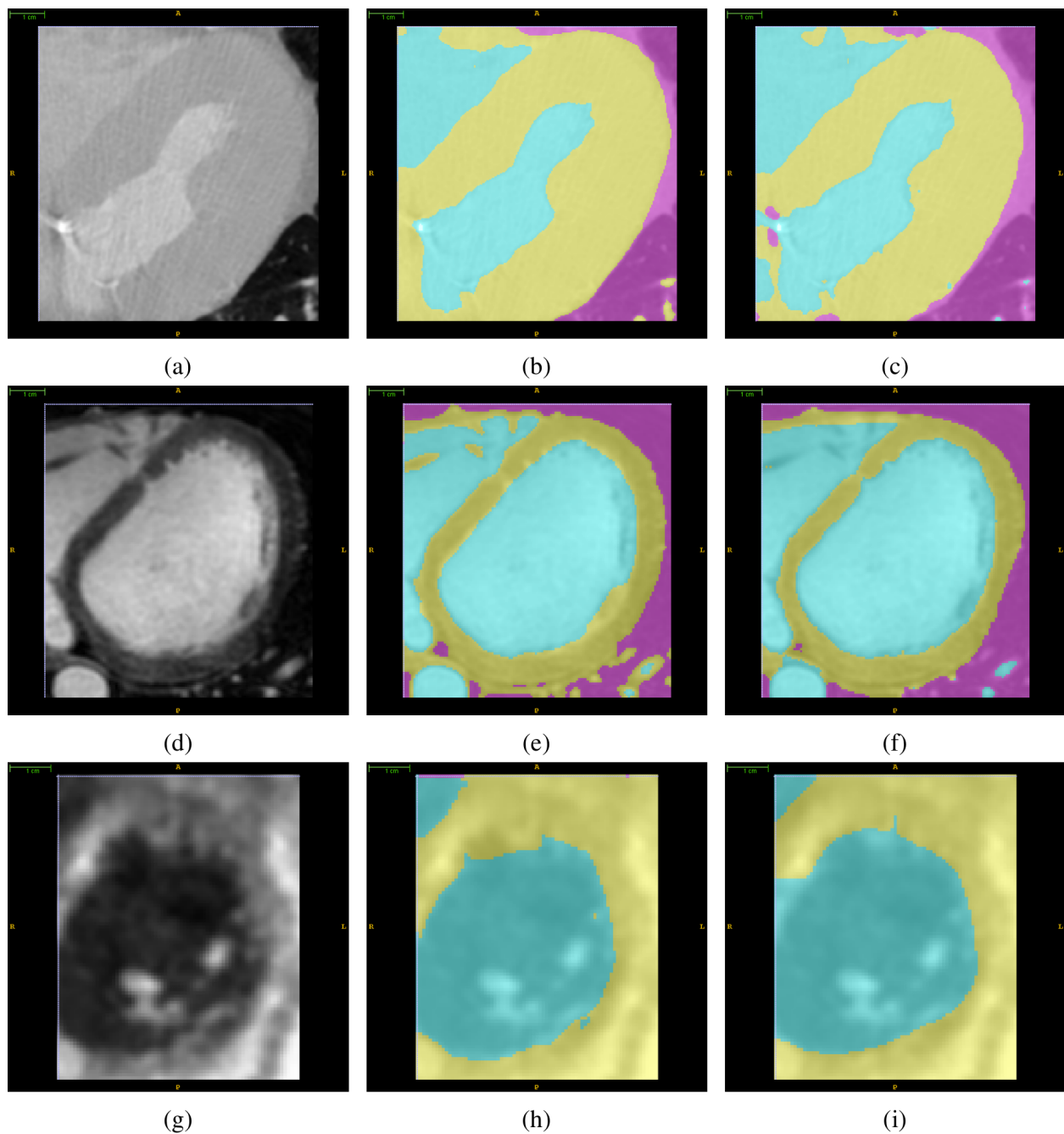


Fig 2: Cardiac segmentation with underlying (a) CT, (d) MRA, and (g) TEE. Manual segmentations are in (b), (e), and (h) respectively, and interactive segmentation results in (c), (f), and (i).

Table 1: Cardiac Segmentation Numerical Results

($n = 3$)		CT	MRA	TEE
Blood AVD	(%)	6.6 ± 6.6	6.2 ± 3.6	14.2 ± 6.2
Myocardium AVD	(%)	12.5 ± 11.3	16.7 ± 11.5	7.3 ± 4.5
Blood rMSE	(mm)	1.14 ± 0.64	0.70 ± 0.21	1.08 ± 0.27
Myocardium rMSE	(mm)	1.31 ± 0.24	0.71 ± 0.24	1.48 ± 0.57
Blood DSC	(%)	91.7 ± 2.6	94.3 ± 1.9	90.5 ± 4.3
Myocardium DSC	(%)	83.8 ± 3.9	82.1 ± 3.7	91.8 ± 2.7
Weighted DSC	(%)	87.5 ± 2.0	89.8 ± 2.7	91.2 ± 3.2
Inter-operator variability				
Weighted DSC	(%)	92.7 ± 4.9	93.6 ± 2.5	92.0 ± 2.1
Weighted DSC from⁹	(%)	87.7 ± 3.7	89.3 ± 2.7	85.7 ± 2.0

Numerical results in terms of average volume difference (AVD), root mean squared distance error (rMSE), and Dice similarity coefficient (DSC) are recorded in Table 1. These results are very consistent with interoperator variability above 90% and comparable with those presented by Rajchl et al.⁹ illustrating that our general-purpose segmentation interface can perform similarly to one designed specifically for cardiac segmentation. Interestingly, the results for TEE indicate that the proposed interface outperforms the previous interactive segmentation interface.⁹

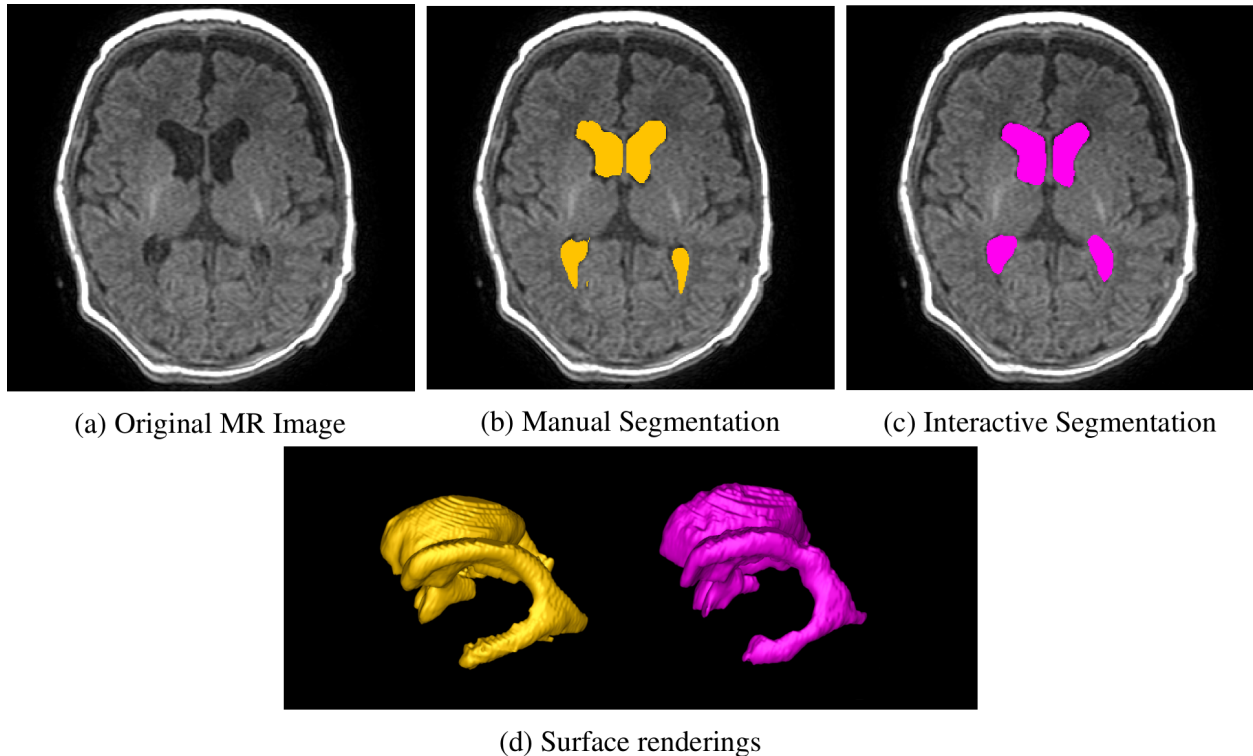


Fig 3: Neonatal Ventricle Segmentation with (a) the MR, (b) the manual segmentation, and (c) interactive segmentation results. (d) shows surface renderings of both the fully manual (left) and interactive (right) segmentation results.

4.2 Neonatal Cranial MRI Segmentation

Neonatal brain images display some unique challenges for automated segmentation in that there are relatively few compared to adult brain images, making machine learning-based or atlas-based segmentation approaches infeasible. In addition, bleeds in the ventricular system further complicated segmentation. In this context, interactive interfaces can be extremely useful since manual segmentation or correction is largely unavoidable. Figure 3 displays visual results of neonatal

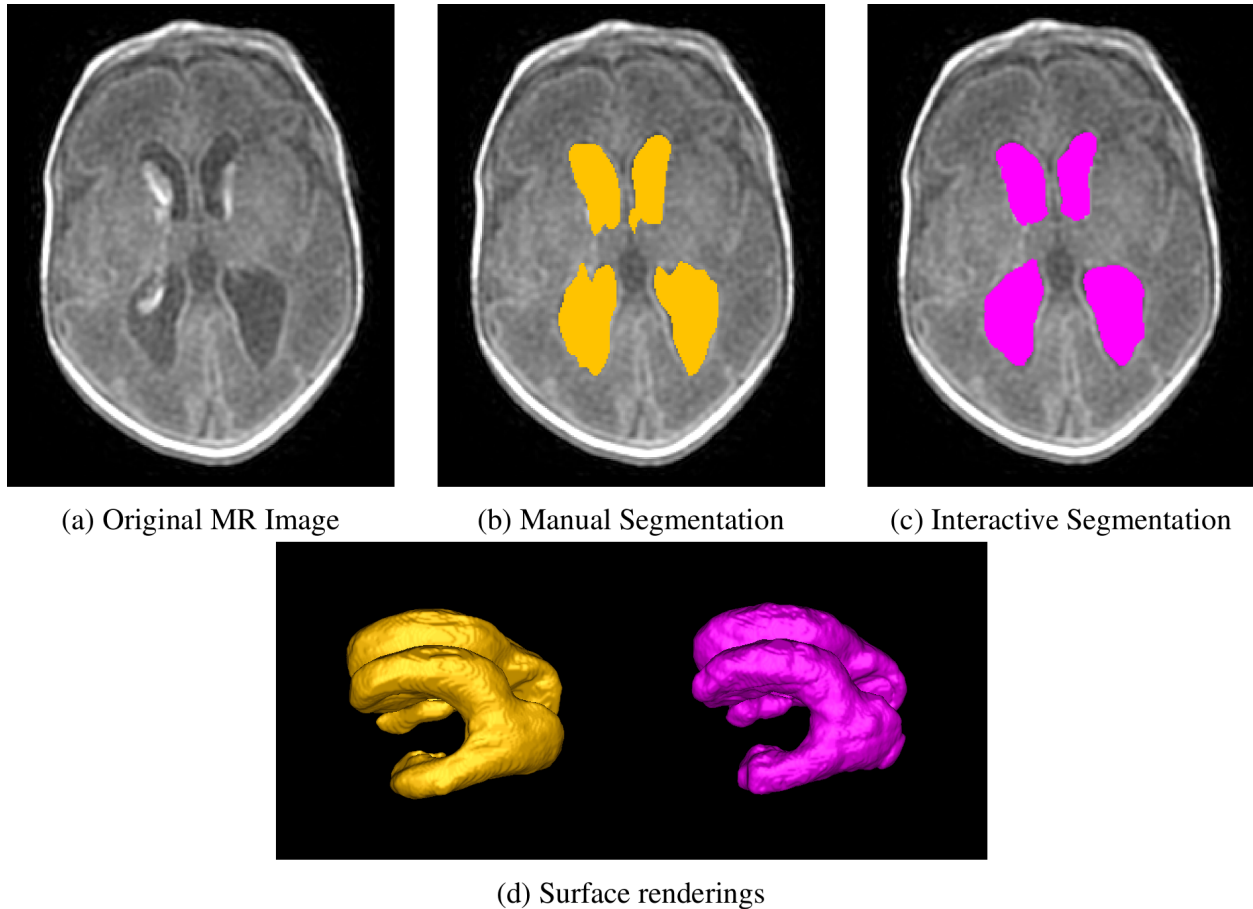


Fig 4: Pathological Neonatal Ventricle Segmentation with (a) the MR, (b) the manual segmentation, and (c) interactive segmentation results. (d) shows surface renderings of both the fully manual (left) and interactive (right) segmentation results.

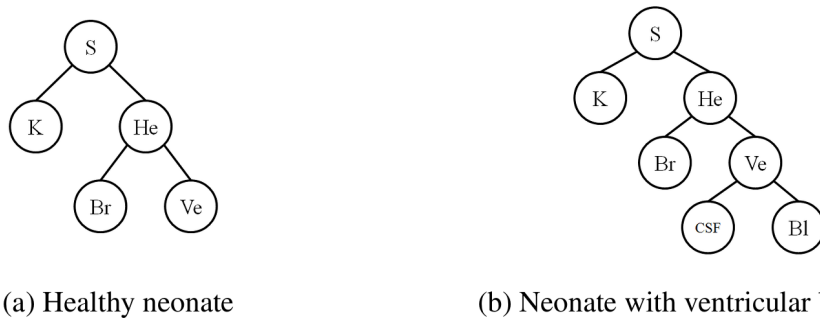


Fig 5: Hierarchies used in (a) healthy and (b) pathological neonatal ventricle segmentation.

ventricle segmentation using this interface.

To demonstrate the interactive segmentation interface’s robustness to pathology, the previous experiment was extended to a neonatal MR image in which a severe ventricular bleed changes the intensity distribution of the ventricle to an extreme degree. The segmentation results are given in Figure 4. Note that the hyper-intense ventricular bleed is closer in intensity to white- and grey-matter than to the ventricles, and it’s appearance on the boundary of the ventricles would likely cause severe registration artifacts. The segmentation of the ventricle was achieved by partitioning it into two components; a healthy component (CSF) and the ventricular bleeding (BI). The union of these components could then be regularized similar to the ventricle (V_e) in Figure 3. The V_e label (the union of the CSF and BI labels) for the pathological case is given in Figure 4 In the hierarchies used in this segmentation problem, which are given in Figure 5, the remaining labels are K which refers to the background, He to the head, and Br to the brain.

5 Automatic Hierarchy Refinement

Although determining an appropriate hierarchy merely from grouping information is a computationally difficult problem, due to the mathematical formulation, it is possible to automatically refine a user-provided hierarchy for improved computational efficiency without compromising segmentation quality. This involves the contraction and removal of vertices in the hierarchy with zero

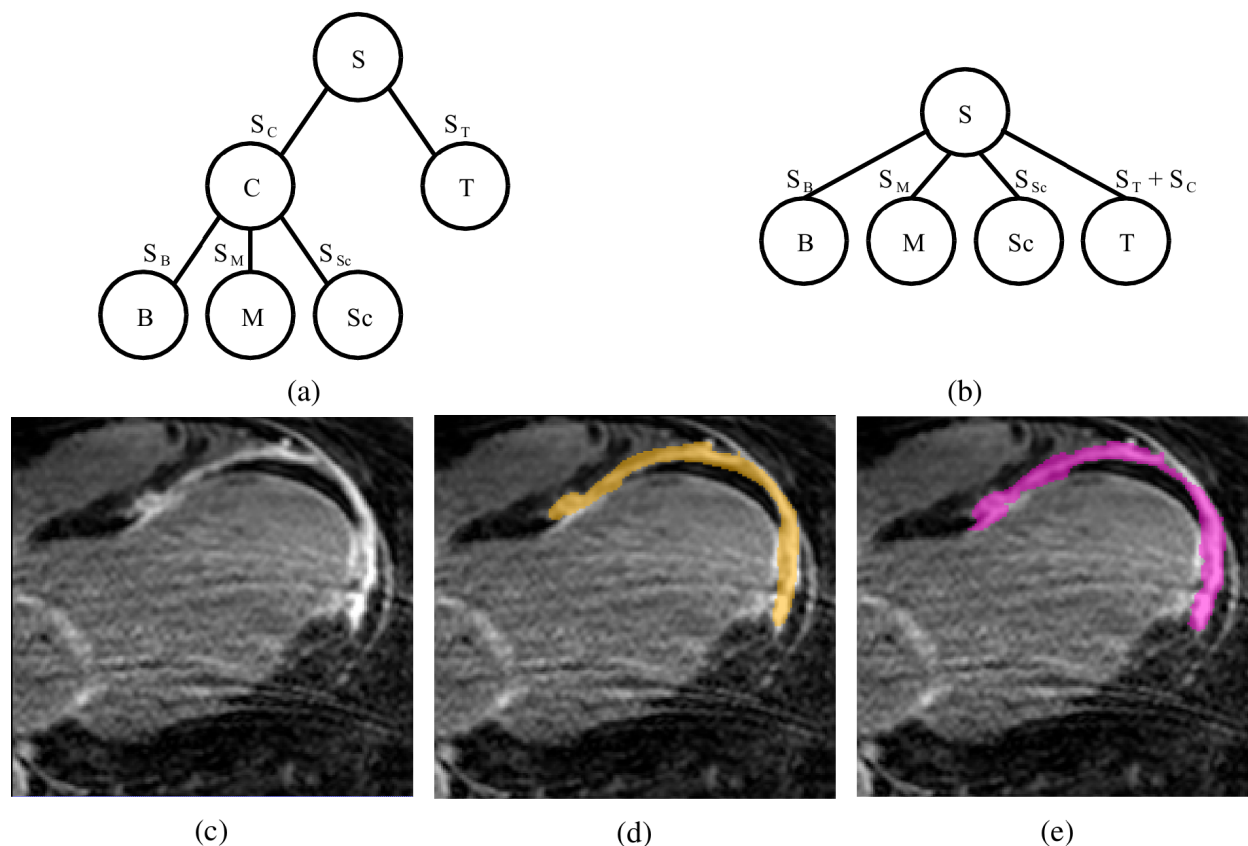


Fig 6: Example of automatic hierarchy segmentation. (a) is the original hierarchy reproduced from¹⁰ and (b) the optimized version, (c) an LGE-MRI with (d) manual segmentation and (e) interactive segmentations results.

regularization or where zero regularization can be induced without changing the optimization functional. One specific example of is that when the source node has only two children, whereby one can be contracted by transferring its smoothness value to the other. To demonstrate this, we performed automatic hierarchy optimization on the method presented by Rachl et al.¹⁰ using Late Gadolinium Enhanced Magnetic Resonance Imaging (LGE-MRI). This segmentation problem involved partitioning the image into thoracic background (T) and cardiac (C) labels, the latter being subdivided into blood (Bl), healthy myocardium (M) and scar tissue (Sc) as shown in Figure 6a. The cardiac label, C, was automatically contracted, resulting in Figure 6b and an estimated 20% improvement in speed.

As with the previous experiments, the results (recorded in Table 2) were comparable to those presented by Rachl et al.¹⁰ and was within the range of inter-operator variability. However, this level of accuracy was achieved without post-processing steps, such as connected components analysis, or other modifications that would make the interface specific to cardiac or LGE-MRI segmentation.

Table 2: Scar Tissue Segmentation Results

$(n = 10)$	Accuracy
Scar AVD (%)	26.9 ± 15.6
Scar rMSE (mm)	1.30 ± 0.32
Scar DSC (%)	74.1 ± 3.5
Scar DSC from¹⁰ (%)	76.0 ± 3.0
Inter-operator variability from¹⁰ - Scar DSC (%)	76.2 ± 2.6
Intra-operator variability from¹⁰ - Scar DSC (%)	75.2 ± 2.8

6 Discussion

Improvements in interactive segmentation interfaces can have a distinct impact in clinical contexts in which automated segmentation is not feasible. Several clinical applications require manual segmentation due to pathology such as tumours in radio-oncological applications or bleeds in neonatal cranial imaging. These applications require a user to manually delineate some anatomy in order to perform relevant measurements such as tumour volume. In these applications, accurate segmentation may be necessary for robust, correct measurements, and the use of interactive segmentation can have a distinct benefit, conserving user time while encouraging accurate results, which will in turn improve patient outcomes by improving the diagnostic capabilities of these measurements (compared to manual segmentation) in single acquisition and longitudinal studies.

The primary advantage of this interface over other interactive segmentation programs is that it allows the user to interactively specify both segmentation hierarchy and initial seeds. The former means that the interface is very general purpose, allowing for arbitrary regions to be defined, while incorporating anatomical knowledge in a direct manner. This gives it a distinct advantage over other interactive segmentation interfaces which either limit the number or type of regions, or do not allow the user to specify abstract anatomical knowledge. The latter takes advantage of a paint-brush mechanism which allows for large regions of the interior of the object to be seeded with minimal user effort thus improving the probabilistic data terms.

The second major advantage is that the algorithm is founded in optimization principles, ensuring robustness and repeatability across images. The formulation of the costs also allow for the regional and boundary uncertainty (U_R and U_B) identified in⁶ to be actively addressed by the segmentation process, making plane selection simpler and more efficient. Plane selection is further improved by selecting only axis-aligned planes in which the user is accustomed.

7 Future Work

There are several future directions in which to take this work aside from general improvements to computational resource usage and performance. Specifically:

- Incorporation of a more extensive model of label organization,
- Incorporation of geometric or shape constraints,
- Improvements to the definition of the smoothness model, and
- Improvements to the plane selection mechanism.

Recently, work has been performed which extends the possibility of label organization in continuous max-flow from hierarchical models¹⁵ to models that allow for any possible label ordering.²² However, there remain issues in terms of how these structures can be specified by a user in runtime in an intuitive manner as they are defined using a constrained set of rooted, weighted directed acyclic graphs, which do not have a user-friendly tool already in place.

There has also been increasing interest in the use of generic geometric or shape constraints such as star-shaped priors in both graph-cuts²³ and max-flow image segmentation.²⁴ Shape complexes have already been proposed which combine the notions of label orderings and star-convex object constraints to develop complicated models of object geometry from the union and disjunction of star-convex objects.²⁵ Such frameworks can be readily incorporated into this interactive segmentation framework with minimal changes to the interface or usability, while contributing a significant improvement to the segmentation accuracy through the encoding of additional anatomical knowledge.

Currently, the interface allows the user to modify the parameters in the smoothness term, but does not permit any other manipulation. This could be incorporated through the addition of a contouring mechanism similar to that in Intelligent Scissors, TurtleSeg, and ITKSnap. These contours could supply specific information which can improve the smoothness terms, as well as give the user complimentary ways to sample regions.

In terms of plane selection, future work could include defining a sequence of planes sensitive to the distance between them, rather than a single set. This would allow the algorithm to intelligently inform the user of multiple areas of uncertainty without re-invoking the continuous max-flow segmentation algorithm and allow the user to provide feedback on multiple high uncertainty planes in a single interaction cycle.

8 Conclusions

Interactive segmentation helps bridge the gap between manual and automatic segmentation allowing each to address the weaknesses of the other. In this work, we present a novel general-purpose interactive segmentation interface and applied it to cardiac and neonatal cranial segmentation with performance comparable to previously published methods specific to said applications.

This interface allows for the user to define a segmentation hierarchy in run-time, taking advantage of a fast, GPU-accelerated general HMF solver, which in turn allows for more knowledge of spatial relationships between anatomical regions to be encoded. This encourages the use of optimization techniques and interactive interfaces in which a user can quickly define and correct a segmentation, and thereby increase the speed, quality, and robustness of general segmentation tasks. The ability to modify the hierarchy in run-time allows for the interactive segmentation interface to account for extreme deviations, such as ventricular bleeds, by the addition of multiple labels to account for them. This interface is the first to allow the user to modify the abstract anatomic knowledge, i.e. label ordering, provided to the computer in run-time.

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Appendix: NP-Hardness of Hierarchy Definition

Theorem: Consider \mathbb{L} to be the set of objects in an image. Determining if there is a hierarchy with at least k elements from a specified set of group relationships ($\mathbb{G} \subseteq 2^{\mathbb{L}}$) is NP-complete, and specifying the largest hierarchy is NP-hard.

Proof. Any hierarchy is equivalent to an independent set in a particular, polynomial-time constructible graph. To prove this, we will show the construction of this graph and proceed through a proof by contradiction.

Let G be a graph in which each vertex represents a non-empty set of labels in the segmentation that are expected to have some regularization, that is, their union forms a meaningful structure or their grouping is meaningful. In this graph, edges represent *conflicts* where the vertices refer to sets that are neither embedded (one is a subset of the other) nor disjoint. For the sake of notation, each vertex will be denoted via its corresponding element of \mathbb{G} , the grouping relationship it represents.

Assume there is a hierarchy where the nodes are selected from the vertices of G , but do not form an independent set. Consider the edge between two vertices that indicates a dependency, $e = (g_1, g_2)$. The two adjacent vertices $g_1, g_2 \in \mathbb{G}$ refer to two sets of end-labels that are neither disjoint nor a subset of each other. (That is, both $g_1 \cap g_2$ and $g_1 \setminus g_2$ are non-empty.) Consider label A to be an end-label common to both sets. Note since each is a superset of $\{A\}$, they must correspond to ancestors in the hierarchy and both lie on the direct path from $\{A\}$ to the root of the hierarchy. This implies that one must be an ancestor of the other, which is a contradiction since neither is a superset of the other. Thus, any hierarchy must correspond to an independent set in G .

Without loss of generality, assume G is connected. Each independent set can be transformed into a hierarchy in polynomial time in a top-down manner. At each iteration, we want to grow the hierarchy by the vertices corresponding to the largest group of end-labels at the lowest tier possible.

We do this by ordering the vertices in the independent set by the size of group they represent. Then, perform a breadth-first search through the current tree to find the lowest tier that is a superset of the node under consideration. We grow the hierarchy by adding the group under consideration to the identified part of the hierarchy. We repeat this for each node in the set, initializing the hierarchy as only the root node, equivalent to the full set of end-labels. Lastly, we augment the hierarchy with the end-labels to make it valid.

Since the maximum hierarchy and maximum independent set problems can be reduced to each other in polynomial time determining the largest hierarchy must be NP-hard. \square

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