Optimal Multiple Surface Segmentation with Convex Priors in Irregularly Sampled Space

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Abstract—Optimal surface segmentation is a state-of-the-art method used for segmentation of multiple globally optimal surfaces in volumetric datasets. The method is widely used in numerous medical image segmentation applications. However, nodes in the graph based optimal surface segmentation method typically encode uniformly distributed orthogonal voxels of the volume. Thus the segmentation cannot attain an accuracy greater than a single unit voxel, i.e. the distance between two adjoining nodes in graph space. Segmentation accuracy higher than a unit voxel is achievable by exploiting partial volume information in the voxels which shall result in non-equidistant spacing between adjoining graph nodes. This paper reports a generalized graph based optimal multiple surface segmentation method with convex priors which segments the target surfaces in irregularly sampled space. The proposed method allows non-equidistant spacing between the adjoining graph nodes to achieve subvoxel accurate segmentation by utilizing the partial volume information in the voxels. The partial volume information in the voxels is exploited by computing a displacement field from the original volume data to identify the subvoxel accurate centers within each voxel resulting in non-equidistant spacing between the adjoining graph nodes. The smoothness of each surface modelled as a convex constraint governs the connectivity and regularity of the surface. We employ an edge-based graph representation to incorporate the necessary constraints and the globally optimal solution is obtained by computing a minimum $\text{s-t cut}$. The proposed method was validated on 25 optical coherence tomography image volumes of the retina and 10 intravascular multi-frame ultrasound image datasets for subvoxel and super resolution segmentation accuracy. In all cases, the approach yielded highly accurate results. Our approach can be readily extended to higher-dimensional segmentations.

Index Terms—Graph search, optimal surface, image segmentation, minimum $\text{s-t cut}$, irregularly sampled, subvoxel, super resolution segmentation, convex smoothness constraints, optical coherence tomography (OCT), retina, Intravascular ultrasound (IVUS).

1 INTRODUCTION

OVER the recent years, automated segmentation of medical images became an important tool contribution to medical diagnosis and treatment planning. Optimal surface segmentation method for 3-D surfaces representing object boundaries is widely used in image understanding, object recognition and quantitative analysis of volumetric medical images. The optimal surface segmentation technique has been extensively employed for segmentation of complex objects and surfaces, such as knee bone and cartilage, heart, airways and vessels tress, lungs, liver, prostate and bladder, retinal surfaces and fat water decomposition. The segmentation problem is transformed into an energy minimization problem. A graph is then constructed, wherein the graph nodes correspond to the center of evenly distributed voxels (equidistant spacing between adjoining nodes). Edges are added between the nodes in the graph to correctly encode the different terms in the energy function. The energy function can then be minimized using a minimum $\text{s-t cut}$. The resultant minimum $\text{s-t cut}$ corresponds to the surface position of the target surface in the voxel grid.

The method requires appropriate encoding of primarily the following three types of energy terms into the graph construction. The data term (also commonly known as the data cost term) which measures the inverse likelihood of all voxels on a surface, a surface smoothness term (surface smoothness constraint) which specifies the regularity of the target surfaces and a surface separation term (surface separation constraint) which governs the feasible distance between two adjacent surfaces. A detailed description of the energy terms is provided in Section 2. Various types of surface smoothness and surface separation constraints are used for simultaneous segmentation of multiple surfaces. Optimal surface detection method uses hard smoothness constraints that are a constant in each direction to specify the maximum allowed change in surface position of any two adjacent voxels on a feasible surface. It uses hard surface separation constraints to specify the minimum and maximum allowed distances between a pair of surfaces. Methods employing trained hard constraints use prior term to penalize local changes in surface smoothness and surface separation. The constraints can also be modelled as a convex function (convex smoothness constraints) as reported in Ref. 19, 22. Furthermore, a truncated convex function (truncated convex constraints) may also be used to
model the surface smoothness and surface separation constraints \cite{23, 24, 20} to segment more complex surfaces but does not guarantee global optimality. A truncated convex constraint enforces a convex function based penalty with a bound on the maximum possible penalty.

However, since volumetric data is typically represented as an orthogonal matrix of intensities, the surface segmentation cannot achieve a precision greater than a single unit voxel, i.e. the distance between two adjoining nodes in the graph space. Accuracy higher than a single unit voxel (subvoxel accuracy) can be attained by exploiting the partial volume effects in the image volumes \cite{25, 26} which leads to non-equidistant spacing between the adjoining graph nodes resulting in an irregularly sampled space. Volumetric images are obtained by discretizing the continuous intensity function uniformly sampled by sensors, resulting in partial volume effects \cite{27, 28}. Partial volume effects are inherent in images and is pronounced when the image acquisition spatial resolution is not high enough, resulting in voxels containing partial information from various features (like tissues) of the imaged object. Even if the imaging system has perfect spatial resolution, there is still some partial volume effect because of image sampling \cite{29}. The partial volume effects are ignored if the intensity or the gradient is measured at the center of each voxel to assign the costs and the graph is created with equidistant nodes. The ignored partial volume information can be utilized by computing a displacement field directly from the volumetric data \cite{25} to identify the subvoxel accurate location of the centers within each voxel, thus requiring a generalized construction of the graph with non-equidistant spacing between orthogonal adjoining nodes (irregularly sampled space). Subvoxel segmentation accuracy attained by exploiting the partial volume effects allows better diagnosis and treatment of disease. Consequently, equivalent segmentation accuracy with lower resolution image acquisition hardware allows for more cost-effective imaging.

The optimal surface segmentation technique employing the different types of smoothness constraints as discussed above is not capable of segmenting surfaces with subvoxel accuracy in a volume which requires segmentation in a grid comprising of non uniformly sampled voxels where the spacing between the orthogonally adjoining nodes is non-equidistant.

To address this problem, the subvoxel accurate graph search method \cite{25} was developed to simultaneously segment multiple surfaces in a volumetric image by exploiting the additional partial volume information in the voxels. A displacement field is computed from the original volumetric data. The method first creates the graph using the conventional optimal surface segmentation method \cite{1}, then deforms it using a displacement field and finally adjusts the inter-column edges and inter-surface edges to incorporate the modification of these constraints. Specifically, such a deformation shall result in non-equidistant spacing between the adjoining nodes which may be considered equivalent to a generalized case of a cube volume formed by non-uniform sampling along the z dimension for the purposes of 3-D surface segmentation. The method demonstrated achievement of subvoxel accuracy compared to the traditionally used optimal surface segmentation method \cite{1}. An example is shown in Fig. 1. However, the method employs hard surface smoothness which does not allow flexibility in constraining surfaces. Specifically, the method is not capable of incorporating a convex surface smoothness constraint in the graph with non-equidistant spacing between adjoining nodes.

Our main contribution is extension of the framework presented in Ref. \cite{25} to incorporate convex surface smoothness constraints for multiple surface segmentation in irregularly sampled space. The proposed method is a generalization of the graph based optimal surface segmentation with convex priors \cite{19} in the regularly sampled space. Consequently, the graph constructed in the regularly sampled space forms a special case in the irregularly sampled space framework where the spacing between the adjoining nodes is set to be a constant (equidistant). Usage of a convex prior allows for incorporation of many different prior information in the graph framework as discussed previously while attaining subvoxel accuracy. Unlike the subvoxel accurate graph search method \cite{25}, the proposed method does not require a two step process to create the graph by the conventional method and then readjust the edges, but instead provides a one step function to add edges between nodes from two neighboring columns to incorporate the convex prior. The proposed method provides the globally optimal solution by directly solving the problem in the irregularly sampled space which fundamentally distinguishes the approach from the local adjustments made to the segmentation in the regularly sampled space as reported in \cite{25}.

In the following sections, we briefly explain the formulation for the optimal surface segmentation method in the regularly sampled space, explain the formulation and description of our novel graph construction to incorporate the convex smoothness constraints in the irregularly sampled space. Next, the evaluation is performed on the spectral domain optical coherence tomography volumes of the retina and intravascular multi-frame ultrasound image datasets for validation and applicability of the method to demonstrate subvoxel and super resolution segmentation accuracy compared to optimal surface segmentation method.
with convex priors in regularly sampled space [19]. Finally, the proof for correctness of graph construction to model the convex surface smoothness constraints is presented in Appendix A and B.

2 METHODS

For ease of understanding, we first briefly recall the formulation of the original optimal surface segmentation method. Then the formulation for the proposed method is presented by building upon the formulation of the original optimal surface segmentation method.

2.1 Problem Formulation and Energy Function

The problem formulation for the widely used optimal surface segmentation methods [1] [21] [19] is described as follows. Consider a volume \( I(x,y,z) \) of size \( X \times Y \times Z \). A surface is defined as a function \( S(x,y) \), where \( x \in \{0,1,\ldots,X-1\} \), \( y \in \{0,1,\ldots,Y-1\} \) and \( S(x,y) \in z = \{0,1,\ldots,Z-1\} \). It is worth noting that the center of voxels is uniformly sampled. Each \((x,y)\)-pair corresponds to a voxel column \( \{ (I(x,y,z) | z = 0,1,\ldots,Z-1 \} \). We use \( a \) and \( b \) to denote two columns corresponding to two neighbouring \((x,y)\)-pairs in the domain \( x \times y \) and \( N_s \) to denote the neighbourhood setting of image domain. The function \( S(a) \) can be viewed as labeling for \( a \) with the label set \( z \) \( (S(a) \in z) \). For simultaneously segmenting \( \lambda(\lambda \geq 2) \) distinct but interrelated surfaces, the goal of the problem is to seek the globally optimal surfaces \( S_i(a) \), where \( i = 1,2,\ldots,\lambda \) in \( I \) with minimum separation \( d_{j,j+1} \) where \( j = 1,2,\ldots,\lambda-1 \) between each adjacent pair of surfaces \( S_j \) and \( S_{j+1} \).

The problem is transformed into an energy minimization problem. The energy function \( E(S) \) takes the following form as shown in Eqn. [1]:

\[
E(S) = \sum_{i=1}^{\lambda} \left( \sum_{a \in x \times y} D_1(S_i(a)) + \sum_{(a,b) \in N_s} V_{ab}(S_i(a), S_i(b)) \right) + \sum_{i=1}^{\lambda-1} \sum_{a \in x \times y} H_a(S_{i+1}(a), S_i(a))
\]  

(1)

The data cost term \( \sum_{a \in x \times y} D_1(S_i(a)) \) measures the total cost of all voxels on a surface \( S_i \). The surface smoothness term \( \sum_{(a,b) \in N_s} V_{ab}(S_i(a), S_i(b)) \) constrains the connectivity of a surface in 3-D and regularizes the surface. Intuitively, this defines how rigid the surface is. The surface separation term \( H_a(S_i(a), S_{i+1}(a)) \) constrains the distance of surface \( S_i \) to \( S_{i+1} \). A variety of surface smoothness functions have been used for various applications as discussed in Section [1]. The energy function is appropriately encoded in a graph. A minimum \( s-t \) cut is then computed on the graph to get the solutions for the target surfaces \( S_i \).

Typically graph construction is done with equidistant spacing between the adjoining nodes (regularly sampled space). Our main contribution is to allow for optimal surface segmentation in the irregularly sampled space with convex surface smoothness constraints by allowing non-equidistant spacing between the nodes.

We formulate the multiple surface segmentation problem in a similar manner for the irregularly sampled space. Consider a volume \( I(x,y,z) \) where \( x \in x = \{0,1,\ldots,X-1\} \), \( y \in y = \{0,1,\ldots,Y-1\} \) and \( z \in z \in \mathbb{R} \). Each \((x,y)\)-pair corresponds to a column \( \{ (I(x,y,z) | z \in \mathbb{R} \} \), denoted by \( col(x,y) \). Assume each \( col(x,y) \) has exactly \( Z \) elements obtained by sampling strictly in the increasing order along the \( z \) direction, resulting in the volume \( I(x,y,z) \) of size \( X \times Y \times Z \), where \( x \in x = \{0,1,\ldots,X-1\} \), \( y \in y = \{0,1,\ldots,Y-1\} \) and \( z \in z = \{0,1,\ldots,Z-1\} \), thus possibly allowing for non-equidistant spacing between two adjacent elements in the column. As discussed previously \( a \) and \( b \) are used to denote two neighbouring columns.

We define a mapping function for each column \( a \) as \( L_a : \{0,1,\ldots,Z-1\} \rightarrow \mathbb{R} \) which maps the index of sampled points in \( I(a,z) \) to \( I(a,z) \). For example, \( L_a(i) \) denotes the \( z \) coordinate of the \( i+1 \)-th sample along column \( a \), and \( L_a(i+1) > L_a(i) \) because of the strictly increasing order of sampling along column \( a \). An example is shown in Fig. 2. Further, a surface function for column \( a \) is defined as \( S(a) \), where \( S(a) \in z = \{0,1,\ldots,Z-1\} \). The function \( L_a(S(a)) \) can be viewed as labeling for surface \( S(a) \) with the label set \( \mathbb{R} \) \( (L_a(S(a)) \in \mathbb{R}) \). For simultaneously segmenting \( \lambda(\lambda \geq 2) \) surfaces, the goal of the problem is to seek the labeling for surfaces \( L_a(S_i(a)) \) where \( i = 1,2,\ldots,\lambda \) in \( I \) with minimum separation \( d_{j,j+1} \) where \( j = 1,2,\ldots,\lambda-1 \) between adjacent pair of surfaces. It is to be noted, that the surfaces are ordered, i.e. \( L_a(S_{i+1}(a)) \geq L_a(S_i(a)) \).

The corresponding energy function for this formulation is shown in Equation [2].

\[
E(S) = \sum_{i=1}^{\lambda} \left( \sum_{a \in x \times y} D_1(L_a(S_i(a))) + \sum_{(a,b) \in N_s} V_{ab}(L_a(S_i(a)), L_b(S_i(b))) \right) + \sum_{i=1}^{\lambda-1} \sum_{a \in x \times y} H_a(L_a(S_{i+1}(a)), L_a(S_i(a)))
\]  

(2)

Herein, the surface smoothness term is modelled as a convex function as shown in Equation [3].

\[
V_{ab}(L_a(S_i(a)), L_b(S_i(b))) = \psi(L_a(S_i(a)) - L_b(S_i(b)))
\]  

(3)

where, \( \psi(\cdot) \) is a convex function, and without loss of generality, we assume that \( \psi(0) = 0 \) [21].

The surface separation term is modelled as a hard constraint for enforcing the minimum separation between a pair of surfaces as shown in Equation [4].

\[
H_a(L_a(S_{i+1}(a)), L_a(S_i(a))) = \begin{cases} 
\infty, & \text{if } L_a(S_{i+1}(a)) - L_a(S_i(a)) < d_{i,i+1} \\
0, & \text{otherwise} 
\end{cases}
\]  

(4)

where \( d_{i,i+1} \) is the minimum separation between a pair of adjacent surfaces. The method is also capable of incorporating a convex surface separation penalty while enforcing a minimum separation constraint in the irregularly sampled space using the same framework and is discussed in Section [5].
below it and an edge with $D_i(L_\alpha(z - 1))$ weight in the opposite direction. Additionally, an edge with $+\infty$ weight is added from the source node $s$ to each node $n_i(a, 0)$ and an edge with $D_i(L_\alpha(Z - 1))$ weight is added from node $n_i(a, Z - 1)$ to the terminal node $t$.

Any $s$-$t$ cut with finite cost contains only one of the finite weight edges $D_i(L_\alpha(_i))$ for each column $a$, thus enforcing surface monotonicity. This is because, if any $s$-$t$ cut included more than one finite weight edges, then by construction it must include at least one infinite weight edge thereby making its cost infinite. Therefore, any finite $s$-$t$ cut shall intersect each column exactly one time.

2.2.2 Inter-column Edges

Inter-column arcs are added between pairs of neighbouring columns $a$ and $b$ to each subgraph $G_i$ to encode the surface smoothness term. For the purpose of this paper the incorporation of a convex smoothness term is presented. Denote a function operator $f(r_1, r_2)$ as shown in Equation (5).

$$f(r_1, r_2) = \begin{cases} 0, & \text{if } r_1 < r_2 \\ \psi(r_1 - r_2), & \text{otherwise} \end{cases}$$

where $\psi(.)$ is a convex function.

A general weight setting function $g(.)$ is used for the inter-column edges between two neighboring columns. The following inter-column edges are added:

For all $k_1 \in [0, Z - 1]$ and $k_2 \in [1, Z - 1]$, a directed edge with weight setting $g(k_1, k_2)$ as shown in Equation (6) is added from node $n_i(a, k_1)$ to node $n_i(b, k_2)$. Additionally, a directed edge is added from node $n_i(a, k_1)$ to terminal node $t$ with weight setting $g(k_1, Z)$.

$$g(k_1, k_2) = f(L_\alpha(k_1), L_\alpha(k_2 - 1)) - f(L_\alpha(k_1 - 1), L_\alpha(k_2 - 1)) - f(L_\alpha(k_1), L_\alpha(k_2)) + f(L_\alpha(k_1 - 1), L_\alpha(k_2))$$

(6)

Where, if $k_1 = 0$, then $k_1 - 1 \notin \mathbf{z}$, therefore $f(L_\alpha(k_1 - 1), L_\alpha(k_2 - 1)) = f(L_\alpha(k_1 - 1), L_\alpha(k_2)) = 0$ and if $k_2 = Z$, then $k_2 \notin \mathbf{z}$, therefore $f(L_\alpha(k_1), L_\alpha(k_2)) = f(L_\alpha(k_1 - 1), L_\alpha(k_2)) = 0$.

Lemma 1: For any $k_1$ and $k_2$, the function $g(k_1, k_2)$ is non-negative. (Proof in Appendix A)

In a similar manner, for all $k_1 \in [0, Z - 1]$ and $k_2 \in [1, Z - 1]$, edges are constructed from nodes $n_i(b, k_1)$ to nodes $n_i(a, k_2)$ with weight setting $g(k_1, k_2)$ as shown in Equation (7). Additionally a directed edge is added from node $n_i(b, k_1)$ to terminal node $t$ with weight setting $g(k_1, Z)$.

$$g(k_1, k_2) = f(L_\alpha(k_1), L_\alpha(k_2 - 1)) - f(L_\alpha(k_1 - 1), L_\alpha(k_2 - 1)) - f(L_\alpha(k_1), L_\alpha(k_2)) + f(L_\alpha(k_1 - 1), L_\alpha(k_2))$$

(7)

It should be noted that weight setting function $g(k_1, k_2)$ in Equation (7) is similar to Equation (6) with only the
Type III

40

E

I

III

315

90

72

III

88

II

9

E

I

III

III

72

E

1

20

90

III

E

E

I

node as described in Ref. [25] from column surfaces is enforced by adding edges in a similar manner.

Thus the surface smoothness term $V_{ab}(.)$ is correctly encoded in graph $G$.

Example of a graph construction of two neighbouring columns $a$ and $b$ for a given surface with enforcement of convex surface smoothness constraint is shown in Fig.3. Herein, an edge from $n_i(a,k_1)$ to node $n_i(b,k_2)$ is denoted as $E_i(a_k_1,b_k_2)$ for the $i$-th surface. For clarity, an edge $E_i(a_k_1,b_k_2)$ is denoted as Type I if $k_2 > k_1$, as Type II if $k_2 = k_1$ and as Type III if $k_2 < k_1$. The respective edge weights in the graph are summarized in Table 1. The convex function used in the example is a quadratic, taking the form $\psi(k_1 - k_2) = (k_1 - k_2)^2$.

The following can be verified from the example shown in Fig.3

- The correct cost of cut $C_1 = (21 - 12)^2 = 81$. It can be verified that the inter-column edges contributing to the cost of cut $C_1$ are Type I edges $E(a_2,b_3)$ and $E(a_1,b_3)$. Summing the edge weights from Table 1 cost of cut $C_1 = 65 + 16 = 81$.
- The correct cost of cut $C_2 = (25 - 37)^2 = 144$. It can be verified that the inter-column edges contributing to the cost of cut $C_2$ are Type I edges $E(b_1,a_5), E(b_3,a_4)$ and Type II edge $E(b_4,a_3)$. Summing the edge weights from Table 1 cost of cut $C_2 = 9 + 9 + 126 = 144$.
- The correct cost of cut $C_3 = (25 - 3)^2 = 484$. It can be verified that the inter-column edges contributing to the cost of cut $C_3$ are Type I edges $E(a_0,b_2), E(a_1,b_2), E(a_1,b_3), E(a_2,b_3)$, Type II edges $E(a_3,b_3), E(a_2,b_2)$ and Type III edge $E(a_3,b_2)$. Summing the edge weights from Table 1 cost of cut $C_3 = 1 + 152 + 16 + 65 + 88 + 90 + 72 = 484$.
- The correct cost of cut $C_4 = (25 - 1)^2 = 576$. It can be verified that the inter-column edges contributing to the cost of cut $C_4$ are Type I edges $E(a_0,b_1), E(a_0,b_2), E(a_1,b_2), E(a_1,b_3), E(a_2,b_3)$, Type II edges $E(a_3,b_3), E(a_2,b_2), E(a_1,b_1)$ and Type III edges $E(a_3,b_2), E(a_3,b_1), E(a_2,b_1)$. Summing the edge weights from Table 1 cost of cut $C_4 = 8 + 1 + 152 + 16 + 65 + 88 + 90 + 48 + 72 + 16 + 20 = 576$.

It can be verified, that no finite $s$-$t$ cut is possible when $L_a(z) - L_a(z) < d_{i,i+1}$, since by construction an intersurface edge of $+\infty$ weight will be cut, thus making the cost infinite. An example of a graph construction for two corresponding columns of adjacent pair of surfaces with enforcement of the surface separation constraint is shown in Fig.4.

Thus the surface separation term $H_a(.)$ is correctly encoded in graph $G$.

2.3 Surface Recovery from Minimum $s$-$t$ cut

The minimum $s$-$t$ cut in the graph uniquely defines optimal $\lambda$ surfaces $S_i$ where $i = 1, 2 \ldots \lambda$. For a given surface $S_i$, the surface location for each col $(x,y) \in z$, where $x \in x$ and $y \in y$ is given by the minimum $s$-$t$ cut. The final surface positions for each column $a$ is recovered by applying the mapping function $L_a : \{0, 1, \ldots , Z - 1\} \rightarrow R$, where $a \in x \times y$, thereby yielding the resultant surface positions for each column $L_a(S_i(a)) \in \hat{z}$, where $\hat{z} \in R$.

3 EXPERIMENTAL METHODS

In this section, we present the application of our method on Spectral Domain Optical Coherence Tomography (SD-OCT) volumes to segment multiple surfaces simultaneously with subvoxel and super resolution segmentation accuracy. The proposed method was also applied to Intravascular Ultrasound (IVUS) images for Lumen and Media segmentation with subvoxel accuracy. The experiment conducted on the SD-OCT volumes have a twofold objective. The first experiment is designed to demonstrate multiple surface segmentation with convex priors while achieving subvoxel accuracy. The second experiment is used to show that the proposed method has the potential to perform super resolution segmentation with sufficient accuracy, i.e achieve adequate segmentation accuracy by operating in the downsampled version of data as compared to segmenting the data.

| Edge       | Type | Weight | Edge       | Type | Weight |
|------------|------|--------|------------|------|--------|
| $E(a_0,b_1)$ | I    | 8      | $E(b_2,a_1)$ | III  | 64     |
| $E(a_0,b_2)$ | I    | 1      | $E(b_2,a_1)$ | III  | 368    |
| $E(a_1,b_1)$ | II   | 48     | $E(b_2,a_2)$ | III  | 95     |
| $E(a_1,b_2)$ | I    | 152    | $E(b_3,a_3)$ | II   | 40     |
| $E(a_1,b_3)$ | I    | 16     | $E(b_3,a_4)$ | I    | 9      |
| $E(a_2,b_1)$ | III  | 20     | $E(b_1,a_1)$ | III  | 216    |
| $E(a_2,b_2)$ | II   | 90     | $E(b_1,a_2)$ | III  | 90     |
| $E(a_2,b_3)$ | I    | 65     | $E(b_1,a_3)$ | III  | 72     |
| $E(a_3,b_1)$ | III  | 16     | $E(b_1,a_4)$ | II   | 126    |
| $E(a_3,b_2)$ | III  | 72     | $E(b_1,a_5)$ | I    | 9      |
| $E(a_3,b_3)$ | III  | 88     | $E(b_2,a_3)$ | III  | 312    |
| $E(a_4,b_1)$ | III  | 36     | $E(b_2,a_2)$ | III  | 130    |
| $E(a_4,b_2)$ | III  | 162    | $E(b_2,a_3)$ | III  | 104    |
| $E(a_4,b_3)$ | III  | 279    | $E(b_2,a_4)$ | III  | 234    |
| $E(a_4,b_4)$ | III  | 36     | $E(b_2,a_5)$ | II   | 247    |
| $E(a_5,b_1)$ | III  | 72     |               |      |        |
| $E(a_5,b_2)$ | III  | 324    |               |      |        |
| $E(a_5,b_3)$ | III  | 576    |               |      |        |
| $E(a_5,b_4)$ | III  | 315    |               |      |        |
| $E(a_5,b_5)$ | II   | 221    |               |      |        |
| $E(a_5,b_6)$ | I    | 4      |               |      |        |

2.2.3 Inter-surface Edges

The surface separation term $H_a(.)$ between two adjacent surfaces is enforced by adding edges in a similar manner as described in Ref. 25 from column $a$ in subgraph $G_i$ to corresponding column $a$ in subgraph $G_{i+1}$. Along every column $a$ in $G_i$, each node $n_i(a,z)$ has a directed edge with $+\infty$ weight to the node $n_{i+1}(a,z')$, if $z' \in Z, L_a(z') - L_a(z) \geq d_{i,i+1}, L_a(z' - 1) - L_a(z) < d_{i,i+1}$. Additionally an edge with $+\infty$ weight is added from node $n_i(a,z)$ to the terminal node $t$ if $L_a(Z - 1) - L_a(z) < d_{i,i+1}$.
in the original resolution with convex surface smoothness constraints.

3.1 Spectral Domain Optical Coherence Tomography (SD-OCT) Volumes of Normal Eye

To demonstrate the utility of our method in simultaneous segmentation of multiple surfaces, three surfaces were simultaneously segmented in this study. The surfaces are $S_1$ - Internal Limiting Membrane (ILM), $S_2$ - Inner Aspect of Retinal Pigment Epithelium Drusen Complex (IRPEDC) and $S_3$ - Outer Aspect of Bruch Membrane (OBM) as shown in Fig. 5.

As discussed earlier Abrámoff et al. [25] exploited the additional information contained in the partial volume effect by generalizing the graph by applying a deformation field (allowing non-equidistant spacing between nodes) to achieve subvoxel accuracy. The method used hard smoothness constraints to model the surface smoothness term. Our method is directly applicable to such cases and allows for usage of a convex smoothness penalty for surface smoothness. In other words, our method can be used to achieve subvoxel accuracy or super resolution accuracy with a convex smoothness penalty term. In this experiment we compare the segmentation accuracy of the proposed method.
3.1.2 Workflow

The original SD-OCT volumes first undergo pre-processing which involves the application of a $10 \times 10 \times 10$ median filter followed by a $10 \times 10 \times 10$ Gaussian filter with a standard deviation of 7 to denoise the original data. The resulting volumes are then down-sampled by a factor of 4 in the $x$ direction, followed by a down-sampling by a factor of $\eta$ in the $z$ direction, resulting in input volume data of size $250 \times 100 \times 512$ voxels. Further cost function image volumes $D_{i,\eta}$ ($i = 1, 2, 3$) are generated for each target surface at scale $\eta$ using the input volume data.

Experiment for Subvoxel Accuracy - The down-sampling factor $\eta = 4$ is chosen for this experiment. The cost function image volumes are simultaneously segmented using the OSCS method to obtain the segmentation for comparison with the proposed method. Thereafter, a shift of evenly distributed voxels to deformed space is computed using gradient vector flow (GVF) [31] as described in Section 3.1.4 on the input volume data. The deformation field is then applied to the cost function image volumes to obtain $D'_{i,\eta}$, ($i = 1, 2, 3$) and the shifted position of each voxel center is recorded. More details regarding the application of the deformation field on the cost function image volume can be found in Ref. [33]. Finally, the deformed cost function image volumes $D'_{i,\eta}$, ($i = 1, 2, 3$) are segmented using the proposed method with non-equidistant spacing of the voxel centers based on the shifted voxel centers.

The generated input volume data is used to evaluate segmentation accuracy of the two methods with respect to the subvoxel accurate expert manual tracings. For fair and robust analysis, the deformation obtained from the GVF was applied to the automated segmentations obtained from the OSCS method, resulting in deformed OSCS (DOSCS) segmentations. The quantitative analysis was conducted by comparing the segmentations obtained from the OSCS method, proposed method and DOSCS segmentations with the subvoxel accurate expert manual tracings. The corresponding workflow of the experiment is shown in Fig. 6.

Experiment for Super Resolution Accuracy - In this experiment we down-sample the data to four different scales at $\eta = 2, 4, 6, 8$. The cost function image volume at the original scale ($\eta = 1$) is simultaneously segmented using the OSCS method to obtain the segmentation for comparison with the proposed method. The proposed method is applied to input volume data at the down-sampled scales. The shift of evenly distributed voxels to deformed space at each down-sampling scale is computed using gradient vector flow (GVF) [31] on the input volume data at each scale $\eta$. The deformation field is then applied to the cost function image volumes at their respective scales and the shifted position of each voxel center is recorded. Finally, the deformed cost function image volumes $D'_{i,\eta}$, ($i = 1, 2, 3$ and $\eta = 2, 4, 6, 8$) at each scale $\eta$ are segmented using the proposed method with non-equidistant spacing of the voxel centers based on the shifted voxel centers due to the applied deformation.

The quantitative analysis was conducted by comparing the segmentations obtained from the OSCS method at the original scale and the proposed method at different down-sampling scales with the expert manual tracings. The corre-


3.1.3 Cost Function Design

The cost function image volumes encode the data term shown in Equation 2. To detect surfaces $S_1$ and $S_3$, a 3-D Sobel filter of size $5 \times 5 \times 5$ voxels is applied to generate cost volumes $D_1$ and $D_3$ wherein the vertical edges for dark to bright transitions and bright to dark transitions are emphasized. To detect surface $S_2$, a machine learning based approach is adopted to generate the cost volume for the same. For each voxel $I(x, y, z)$ in an image slice of the input volume data, a $11 \times 11$ window centered at voxel $I(x, y, z)$ is used to generate a feature vector comprising of the intensity values of each voxel in the given window, thus resulting in 121 features. A random forest classifier with 10 trees is then trained on voxels of the training set input image volumes to learn the probability maps which indicate the likelihood of voxel belonging to the surface of interest with respect to the expert manual tracings. The trained classifier is then applied to each voxel of the test set resulting in a probability map $D_2(x, y, z)$. Finally, cost volume $D_2$ to detect $S_2$ is generated by assigning $D_2(x, y, z) = (1 - D_2'(x, y, z)) \times 255$ as voxel intensity.

3.1.4 Gradient Vector Field

A gradient vector field (GVF) is a feature preserving diffusion of the gradient in a given image volume. In this study, GVF is used as a deformation field $F(x, y, z)$ obtained directly from the input volume data acting on the center of each voxel $(x, y, z)$ to shift the evenly distributed voxels to the deformed space. The voxel centers are thus displaced towards the regions where salient transitions of image properties are more likely to occur. The shift of the centers of the voxels is given by Equation 8.

$$ (x', y', z') = (x, y, z) + \lambda F(x, y, z) $$  \hspace{1cm} (8)

where $\lambda$ is a normalization factor. The displacement of each voxel center is confined to the same voxel. Therefore, $F(x, y, z)$ is normalized such that the maximum deformation is equal to half of the voxel size $\delta$. The normalization factor takes the following form as show in Equation 9.

$$ \lambda = \frac{\delta}{2 \times max_{(x,y,z) \in (X,Y,Z)} || F(x, y, z) ||} $$  \hspace{1cm} (9)

3.1.5 Parameter Setting

The same parameters were used for segmenting the three surface by the OSCS method and the proposed method at each scale $n$. A linear (convex) function, $\psi(k_1 - k_2) = |k_1 - k_2|$ was used to model the surface smoothness term $V_{ab}()$. The surface separation term $H_a(.)$ is modelled as a hard constraint for enforcing the minimum separation between a pair of surfaces. The minimum separation parameters used are $d_{1,2} = 15$ and $d_{2,3} = 1$ for $\eta = 4$ in the experiment for subvoxel accuracy. The minimum separation parameters used in the experiment for super resolution accuracy at different scales are: $d_{1,2} = 60$ and $d_{2,3} = 4$ for $\eta = 1$, $d_{1,2} = 30$ and $d_{2,3} = 2$ for $\eta = 2$, $d_{1,2} = 15$ and $d_{2,3} = 1$ for $\eta = 4$, $d_{1,2} = 10$ and $d_{2,3} = 0.8$ for $\eta = 6$, $d_{1,2} = 7$ and $d_{2,3} = 0.5$ for $\eta = 8$.

3.2 Intravascular Ultrasound (IVUS) Images

To study the applicability of the proposed method in a broader range of image segmentation tasks, segmentation of lumen and media with subvoxel accuracy was performed in Intravascular Ultrasound (IVUS) images as shown in Fig. 8.

Atherosclerosis, a disease of the vessel wall, is the major cause of cardiovascular diseases such as heart attack or stroke. Early atherosclerosis results in remodelling, thus retaining the lumen despite plaque accumulation. Atherosclerosis plaque is located between lumen and media that can be identified in IVUS images. Automated IVUS segmentation of lumen and media is of substantial clinical interest and contributes to clinical diagnosis and assessment of plaque.

In this experiment we compare the segmentation accuracy of the lumen and media using the proposed method with the complete set of methods used in the standardized evaluation of IVUS image segmentation. The compared methods are namely, P1 - Shape driven segmentation based on linear projections, P2 - geodesic active contour based segmentation, P3 - Expectation maximization based method, P4 - graph search based method, P5 - Binary classification of distinguishing between lumen and non-lumen regions based on multi-scale Stacked Sequential learning scheme, P6 - Detection of Media border by holistic interpretation of the IVUS image (HoliMab), P7 - Lumen segmentation based on a Bayesian approach, P8 - Sequential detection. Overview of the proposed method and each method’s feature, including whether the algorithm was applied to lumen and/or media, whether the segmentation was done in 2-D or 3-D and whether the method was semi-automated or fully automated is shown in Table 2.

| Method | Category | Automation | 2-D/3-D |
|--------|----------|------------|--------|
| P1     | Lumen and Media | Semi | 2-D |
| P2     | Lumen   | Semi | 2-D |
| P3     | Lumen and Media | Semi | 2-D |
| P4     | Lumen and Media | Fully | 3-D |
| P5     | Lumen   | Fully | 3-D |
| P6     | Media   | Fully | 2-D |
| P7     | Lumen   | Semi | 2-D |
| P8     | Lumen and Media | Fully | 2-D |
| Our method | Lumen and Media | Fully | 3-D |

3.2.1 Data

The data used for this experiment was obtained from the standardized evaluation of IVUS image segmentation database. In this experiment Dataset B as denoted in Ref. was used. The data comprises of a set of 435 images with a size of $384 \times 384$ pixels extracted from in vivo pullbacks of human coronary arteries from 10 patients. The respective expert manual tracings (subvoxel accurate) of lumen and media for the images were also obtained from the reference database. The dataset contains 10 multi-frame datasets, in which 3D context from a full pullback is provided. Each dataset comprises of between 20 and 50 gated frames extracted from the full pullback at the end-diastolic cardiac phase. Further, the obtained data comprised of two...
Original SD-OCT volume (1000 x 100 x 512 voxels)
Pre-processing
Down-sample (250 x 100 x 128 voxels)
GVF
Segmentation using proposed method
Performance evaluation
Expert manual tracings
Map to low resolution (subvoxel accurate expert manual tracings)

Fig. 6. Experiment design for segmentation of SD-OCT volumes of normal eye with subvoxel accuracy.

Original SD-OCT volume (1000 x 100 x 512 voxels)
Down-sample (250 x 100 x 512/n voxels)
GVF
Segmentation using OSCS method
Performance evaluation
Expert manual tracings

Fig. 7. Experiment design for segmentation of SD-OCT volumes of normal eye for super resolution accuracy.

Fig. 8. (a) A single frame of an IVUS multiframe dataset (b) Expert manual tracings of the Lumen (red) and Media (green).

For the IVUS challenge.

3.2.2 Workflow

Each slice of the volumes in the dataset is first converted into a polar coordinate image as shown in Fig 9. The generated “polar image volumes” undergo the application of a $7 \times 7 \times 7$ Gaussian filter with a standard deviation of 4 for denoising. Next, cost function image volumes $D_{\text{lumen}}$ and $D_{\text{media}}$ are generated for the lumen and media respectively. Further the GVF as discussed in Section 3.1.4 is computed on the polar image volumes. The deformation field is then applied to cost function image volumes and the shifted position of the voxel centers are recorded. The deformed cost function image volumes $D'_{\text{lumen}}$ and $D'_{\text{media}}$ are then segmented using the proposed method. Finally the resulting segmentations are mapped back to the original co-ordinate system.

3.2.3 Cost Function Design

To detect the lumen and media, a machine learning approach is adopted. For each pixel of the polar image in

groups - training and testing set. Approximately one fourth of the images in the dataset were grouped in the training set and the remaining were grouped as the testing set, to assure fair evaluation of the algorithms with respect to the expert manual tracings. The experiment with the proposed method was conducted in conformance with the directives provided
the training set, a total of 148 features were generated. The following operators are applied in order to generate the features:

- 16 features are generated by applying a set of 16 Gabor filters to the image according to the following kernel shown in Equation (10).

\[
G(x, y) = \frac{1}{2\pi\sigma_x\sigma_y} e^{-0.5\times((\frac{x}{\sigma_x})^2 + (\frac{y}{\sigma_y})^2) + i2\pi(Ux + Vy)}
\]  

(10)

The parameters U and V (scaling and orientation) used are U = (0.0442, 0.0884, 0.1768, 0.3536), V = (0, π/4, π/2, 3π/4), σ_x = 0.5622U and σ_y = 0.4524U.

- 2 features are generated by applying a 3 × 3 Sobel kernel to the image in the x and y directions.

- 6 features are generated by computing the mean value (m), standard deviation (s) and the ratio m of pixel intensities in a sliding window of size 1 × 10 pixels in the x and y directions.

- 2 features defined as shadow (Sh) and relative shadow (Sr) related to the cumulative gray level of the image are generated as shown in the following Equations (11) and (12).

\[
Sh(x, y) = \frac{1}{N_xN_y} \sum_{y \leq y_i} BI(x, y_i)
\]  

(11)

\[
Sr(x, y) = \frac{1}{N_xN_y} \sum_{y \leq y_i} y_i BI(x, y_i)
\]  

(12)

where BI(x, y) is a binary image obtained by thresholding the image with a thresholding value of 14 and (N_x, N_y) are the image dimensions.

- 1 feature is generated by computing the local binary pattern [45].

- 121 features are generated by using a 11 × 11 window in a similar manner as discussed in Section 3.1.3.

Using the expert manual tracings for the training set two separate random forest classifiers [32] for lumen and media with 10 trees are trained on all the pixels of the images in the training set to learn the probability maps which indicate the likelihood of a pixel belonging to lumen or media respectively. The trained classifiers are then applied to each pixel of the testing set to obtain the two cost function images D_{lumen}, D_{media} for lumen and media in a similar manner as discussed in Section 3.1.3.

3.2.4 Parameter Setting

A linear (convex) function, ψ(k_1 - k_2) = |k_1 - k_2| was used to model the surface smoothness term V_{ab}(·). The surface separation term H_{ab}(·) is modelled as a hard constraint for enforcing the minimum separation between the lumen and media with d_{lumen,media} = 2.

4 RESULTS

4.1 Segmentation of SD-OCT Volumes of Normal Eye

The segmentation accuracy was estimated using unsigned mean surface positioning error (UMSP) and unsigned average symmetric surface distance error (UASSD). The UMSP error for a surface was computed by averaging the vertical difference between the subvoxel accurate manual tracings and the automated segmentations for all the columns in the input volume. The UASSD error for a surface was calculated by averaging the closest distance between all the surface points of the automated segmentation and those of the expert manual tracings in the physical space. Statistical significance of the observed differences was determined using 2-tailed paired t-test for which p values of 0.05 were considered significant.

**Results for subvoxel accuracy** - The USMP errors are summarized in Table 3 and the UASSD errors are summarized in Table 4. Fig. 10 and 11 show the performance comparison of the proposed method, the OSCS method [19] and the DOSCS segmentations. Our method produced significantly lower UMSP and UASSD errors for S_1 (p<0.01), S_2 (p<0.01) and S_3 (p<0.001) compared to the OSCS method and the DOSCS segmentations.

| Surface | OSCS vs. Obsv | DOSCS vs. Obsv | Our method vs. Obsv |
|---------|---------------|----------------|---------------------|
| S_1     | 0.38 ± 0.05   | 0.34 ± 0.05    | 0.23 ± 0.04         |
| S_2     | 0.58 ± 0.37   | 0.57 ± 0.36    | 0.50 ± 0.32         |
| S_3     | 0.93 ± 0.47   | 0.74 ± 0.45    | 0.47 ± 0.43         |
| Overall | 0.63 ± 0.30   | 0.55 ± 0.29    | 0.40 ± 0.26         |

**TABLE 4**

Unsigned average symmetric surface distance error (UASSD) (mean ± standard deviation) in μm. Obsv - Subvoxel accurate expert manual tracings.

| Surface | OSCS vs. Obsv | DOSCS vs. Obsv | Our method vs. Obsv |
|---------|---------------|----------------|---------------------|
| S_1     | 4.91 ± 0.63   | 4.58 ± 0.72    | 3.05 ± 0.55         |
| S_2     | 7.35 ± 3.91   | 7.12 ± 3.76    | 6.51 ± 3.61         |
| S_3     | 12.06 ± 5.03  | 9.10 ± 4.97    | 6.37 ± 4.77         |
| Overall | 8.11 ± 3.19   | 6.93 ± 3.15    | 5.31 ± 2.98         |

Qualitatively the algorithm produced very good and consistent segmentations. The qualitative illustrations are shown in Fig. 13 and 14. In both the illustrations, the first row shows a single B-scan of the input image volume with the subvoxel accurate expert manual tracings and the automated segmentations. The second, third and fourth row show the magnification of the black boxes in the first row corresponding to the surfaces ILM, IRPEDC and OBM respectively. The first column shows the subvoxel...
accurate expert manual tracings. The second column shows
the subvoxel accurate expert manual tracings vs OSCS seg-
mentation. The third column shows the subvoxel accurate
expert manual tracings vs DOSCS segmentation. The fourth
column shows the subvoxel accurate expert manual tracings
vs segmentation from our method.

It can be seen from Fig. 13 and 14 that the proposed
method yields more accurate segmentations compared to
the OSCS method and the DOSCS segmentations for Surface
2 and Surface 3, while from Fig. 14 it can be seen that the
proposed method also yields more accurate segmentation
for Surface 1. Furthermore, the second, third and fourth
rows clearly demonstrates that the proposed method yields
a much higher subvoxel accuracy for the segmentations.
It can be seen from the last row in Fig. 13 that even after
applying the deformation to the OSCS segmentations, the
DOSCS segmentation do not achieve the globally optimum
solution obtained by using the proposed method with sub-
voxel accuracy. This is because all nodes encode potential
surface locations more precisely when the globally optimum
solution is computed in the irregularly sampled graph space
by utilizing the information from the partial volume effect.

Results for super resolution accuracy - The UASSD
errors are summarized in Table 5. The results obtained from
the proposed method at different down-sampling scales
($\eta = 2, 4, 6, 8$) was compared to the segmentation obtained
from the OSCS method at the original scale ($\eta = 1$) to
determine the relative accuracy of the proposed method in
the down-sampled resolutions. The performance of the pro-
posed method compared with the OSCS method for super
resolution segmentation accuracy is shown in Fig. 12. There
was no significant difference between the UASSD errors
produced by the proposed method at $\eta = 2$ and the OSCS
method at original scale ($\eta = 1$) for $S_1$ ($p > 0.05$), $S_2$ ($p > 0.05$)
and $S_3$ ($p > 0.05$). There was no significant difference
between the UASSD errors produced by the proposed method
at $\eta = 4$ and the OSCS method at original scale ($\eta = 1$) for
$S_1$ ($p > 0.05$) and $S_3$ ($p > 0.05$) while there was a significant
difference for $S_2$ ($p < 0.05$). There was a significant difference
observed in between the UASSD errors produced by the
proposed method at $\eta = 6, 8$ and the OSCS method at
original scale ($\eta = 1$) for $S_1$ ($p < 0.05$), $S_2$ ($p < 0.05$) and $S_3$
($p < 0.05$).

In other words, the proposed method achieves adequate
accuracy for down-sampled resolutions at $\eta = 2, 4$ for the
segmented surfaces when compared to the segmentation
accuracy by the OSCS method in the original scale reso-

![Fig. 10. Unsigned mean surface positioning errors observed in 25 vol-
metric OCT images for subvoxel accuracy.](image1)

![Fig. 11. Unsigned average symmetric surface distance errors observed
in 25 volumetric OCT images for subvoxel accuracy.](image2)

![Fig. 12. Unsigned average symmetric surface distance errors observed
in 25 volumetric OCT images for super resolution segmentation accu-
rcy. $\eta$ is the downsampling scale.](image3)

| Surface      | $S_1$          | $S_2$          | $S_3$          |
|--------------|----------------|----------------|----------------|
| OSCS vs. Obsv at $\eta = 1$ | 2.53 ± 0.36 | 5.88 ± 3.28 | 5.81 ± 4.25 |
| Our method vs. Obsv at $\eta = 1$ | 2.69 ± 0.41 | 6.18 ± 3.39 | 6.07 ± 4.41 |
| OSCS vs. Obsv at $\eta = 2$ | 3.05 ± 0.35 | 6.51 ± 3.61 | 6.37 ± 4.77 |
| Our method vs. Obsv at $\eta = 2$ | 3.79 ± 0.94 | 7.58 ± 4.22 | 7.32 ± 5.27 |
| OSCS vs. Obsv at $\eta = 6$ | 5.45 ± 1.71 | 9.15 ± 5.23 | 9.21 ± 6.46 |
| Our method vs. Obsv at $\eta = 6$ | 5.53 ± 2.65 | 9.15 ± 5.23 | 9.21 ± 6.46 |
Fig. 13. Illustration of results on a single B-scan from input image volume. Red - ILM expert tracing, Green - IRPEDC expert tracing, Dark blue - OBM expert tracing, Yellow - ILM automated segmentation, Magenta - IRPEDC automated segmentation, Light blue - OBM automated segmentation.
Fig. 14. Illustration of results on a single B-scan from input image volume. Red - ILM expert tracing, Green - IRPEDC expert tracing, Dark blue - OBM expert tracing, Yellow - ILM automated segmentation, Magenta - IRPEDC automated segmentation, Light blue - OBM automated segmentation.
4.2 Segmentation of Lumen and Media in IUVS Images

The quantitative analysis was carried out by comparing the segmentations obtained by our method with the expert manual tracings (subvoxel accurate). Three evaluation measures were used to quantify the accuracy of the segmentations. We compare the evaluation measures obtained using our method with the measures of methods (P1-P8) reported in Ref. [35]. The measures used are:

- **Jaccard Measure (JM)** - Quantifies how much the segmented area overlaps with the manual delineated area as shown in Equation (13):

\[
JM(R_{\text{auto}}, R_{\text{man}}) = \frac{|R_{\text{auto}} \cap R_{\text{man}}|}{|R_{\text{auto}} \cup R_{\text{man}}|} \tag{13}
\]

where \( R_{\text{auto}} \) and \( R_{\text{man}} \) are two vessel regions defined by the manual annotated contour \( C_{\text{man}} \) and of the automated segmented outline \( C_{\text{auto}} \) respectively.

- **Percentage of Area Difference (PAD)** - Computes the segmentation area difference as shown in Equation (14):

\[
PAD = \frac{|A_{\text{auto}} - A_{\text{man}}|}{A_{\text{man}}} \tag{14}
\]

where \( A_{\text{auto}} \) and \( A_{\text{man}} \) are the vessel areas for the automatic and manual contours respectively.

- **Hausdorff Distance (HD)** - Computes locally the distance between the manual and automated contours as shown in Equation (15):

\[
HD(C_{\text{auto}}, C_{\text{man}}) = \max_{p \in C_{\text{auto}}} \{ \max_{q \in C_{\text{man}}} [d(p, q)] \} \tag{15}
\]

where \( p \) and \( q \) are points of the curves \( C_{\text{auto}} \) and \( C_{\text{man}} \) respectively, and \( d(p, q) \) is the Euclidean distance.

The comparative performance of the proposed method is shown in Figs. [15] [16] and [17]. The results demonstrate that our method performs better than methods P1, P2, P4, P5, P6, P8 and is comparable to methods P3 and P7 with respect to segmentation error measures for lumen and media. Our method segments both the lumen and media simultaneously while method P7 segments the lumen only. Furthermore, our method is fully automated while methods P3 and P7 are semi-automated. Finally, methods P3 and P7 perform slice by slice segmentation in 2-D while our method performs the segmentation in 3-D and not slice by slice.

Qualitative results are shown in Fig. [18]. The illustration demonstrates that our method produced very good segmentation of the lumen and media. It can also be seen from the illustration that the segmentations from our method are consistent for varied topologies of the lumen and media. Constructing the graph with the shifted voxel centers provides a more accurate encoding of the lumen and media surface positions due to the application of the GVF by adaptively changing the regional node density so that it is higher in regions where the target surface is expected to pass through. Employing a subvoxel accuracy approach allows the segmentation to obtain a greater precision with respect to the subvoxel accurate expert tracings.

5 Discussion

A novel approach for segmentation of multiple surfaces with convex priors in irregularly sampled space (non-equidistant spacing between orthogonal adjoining nodes) was proposed. Our method advances the graph based segmentation framework in several important ways. First, the proposed energy function incorporates a convex surface smoothness penalty in irregularly sampled space through a convex function. Second, the approach allows simultaneous segmentation of multiple surfaces in the irregularly sampled space with the enforcement of a minimum separation constraint. Third, our method guarantees global optimality. Lastly, the proposed method demonstrates utility in achieving subvoxel and super resolution segmentation accuracy while employing a convex penalty to model surface smoothness. To the best of our knowledge, this is the first
TABLE 6
Evaluation measures of each method with respect to expert manual tracings. Error measures expressed as mean and (standard deviation). An empty table cell indicates that the method was not applied to Lumen or Media.

| Participant | Lumen | Media |
|-------------|-------|-------|
|             | JM    | PAD   | HD   | JM    | PAD   | HD   |
| P1          | 0.81 (0.12) | 0.14 (0.13) | 0.47 (0.39) | 0.76 (0.13) | 0.21 (0.16) | 0.64 (0.48) |
| P2          | 0.83 (0.08) | 0.14 (0.12) | 0.51 (0.25) |           |       |      |
| P3          | 0.88 (0.05) | 0.06 (0.05) | 0.34 (0.14) | 0.91 (0.04) | 0.05 (0.04) | 0.31 (0.12) |
| P4          | 0.77 (0.09) | 0.15 (0.12) | 0.47 (0.22) | 0.74 (0.17) | 0.23 (0.19) | 0.76 (0.48) |
| P5          | 0.79 (0.08) | 0.16 (0.09) | 0.46 (0.30) |           |       |      |
| P6          |           |       |      | 0.84 (0.10) | 0.12 (0.12) | 0.57 (0.39) |
| P7          | 0.84 (0.08) | 0.11 (0.12) | 0.38 (0.26) |           |       |      |
| P8          | 0.81 (0.09) | 0.11 (0.11) | 0.42 (0.22) | 0.79 (0.11) | 0.19 (0.19) | 0.60 (0.28) |
| Our Method  | 0.86 (0.04) | 0.09 (0.03) | 0.37 (0.14) | 0.90 (0.03) | 0.07 (0.03) | 0.43 (0.12) |

![Fig. 17. Hausdroff distance (HD) metric for IVUS data. Lower HD indicates a closer alignment of the automated and manual segmentations.](image_url)

method that fulfills these three aims at the same time. The hallmark of the proposed method is the ability to perform the segmentation task in an irregularly sampled space which generalizes the optimal surface segmentation framework.

The proposed method is also capable of incorporating convex surface separation penalty while enforcing a minimum separation in the irregularly sampled space. The incorporation of such a penalty would involve modifying the surface separation term in the proposed energy function to impose a convex function based penalty when the minimum separation constraint is not violated. The graph construction to enforce such a penalty can be done using the same framework of the proposed method for enforcing the surface smoothness constraint.

The method can be used in conjunction with the method proposed by Abrámov et. al [25] to incorporate prior information using trained hard and soft constraints [22] to achieve subvoxel accuracy. Furthermore, the method can also be incorporated in the image segmentation framework using truncated convex priors [20] to achieve subvoxel accuracy by constructing the convex part of the graph in the irregularly sampled space, thus providing a potential use for generic modelling of variety of surface constraints to achieve subvoxel accuracy.

The global optimality of the proposed method is evident from the illustration in Fig. 13 and shows that segmentation performed in the irregularly sampled space based on the displacement of the voxel centers to correctly encode the partial volume information is more accurate compared to the segmentation performed without any use of partial volume information. The results on SD-OCT volumes of the retina show that the subvoxel precision is achieved and that the segmentation accuracy compared to the OSCS method and DOSCS segmentations is superior. The results on IVUS images demonstrates that the methods achieves high accuracy with respect to subvoxel accurate expert tracings as compared to the methods reported in the IVUS challenge [35] while being fully automated and performing segmentation in 3-D. The approach is not limited to these two modalities for which the experiments were conducted.

6 Conclusion
We presented a general framework for simultaneous segmentation of multiple surfaces in the irregularly sampled space with convex priors for achievement of subvoxel and super resolution segmentation accuracy. An edge-weighted graph representation was presented and a globally optimal solution with respect to the employed objective function was achieved by solving a maximum flow problem. The surface smoothness and surface separation constraints provide a flexible means for modelling various inherent properties and interrelations of the desired surfaces in an irregularly sampled grid space. The method is readily extensible to higher dimensions.

Appendix A
Proof of Lemma 1
Lemma 1: For any $k_1$ and $k_2$, the function $g(k_1, k_2)$ is non-negative.
Fig. 18. Qualitative illustrations of lumen and media segmentation using our method. Each image is a single frame of an IVUS multiframe dataset. Red - Lumen expert tracing, Green - Media expert tracing, Yellow - Lumen segmentation (our method), Blue - Media segmentation (our method).
Proof: Let us consider the function \( g(k_1, k_2) \) for edges from column \( a \) to neighboring column \( b \) as shown in Equation [16]. We need to prove that \( g(k_1, k_2) \geq 0 \)

\[
g(k_1, k_2) = \frac{f(L_a(k_1), L_b(k_2-1)) - f(L_a(k_1), L_b(k_2)) + f(L_a(k_1-1), L_b(k_2))}{(16)}
\]

The reader should recall because of the strictly increasing order of sampling, \( L_a(k_1) > L_a(k_1-1) \) and \( L_a(k_2) > L_b(k_2-1) \). \( \psi(\cdot) \) is a convex function with \( \psi(0) = 0 \). The proof is presented in a case-by-case basis.

Case 1: \( L_a(k_1) < L_b(k_2-1) \)

Thus, \( L_a(k_1-1) < L_b(k_2-1) \). As \( L_b(k_2) > L_b(k_2-1) \), we have \( L_a(k_1) < L_b(k_2) \) and \( L_a(k_1-1) < L_b(k_2) \). Since \( f(r_1, r_2) = 0 \) if \( r_1 < r_2 \). It is straightforward to verify that \( g(k_1, k_2) = 0 \) in Equation [16].

Case 2: \( L_a(k_1) \geq L_b(k_2-1) \) and \( L_a(k_1) < L_b(k_2) \)

In this case, as \( L_a(k_1) > L_a(k_1-1) \), we have \( L_a(k_1) < L_b(k_2) \). Thus, \( g(k_1, k_2) \) takes the following form in Equation [17].

\[
g(k_1, k_2) = f(L_a(k_1), L_b(k_2-1)) - f(L_a(k_1-1), L_b(k_2-1)) \quad (17)
\]

If \( L_a(k_1) < L_b(k_2-1) \), then

\[
g(k_1, k_2) = f(L_a(k_1), L_b(k_2-1)) = \psi(L_a(k_1) - L_b(k_2-1)).
\]

Thus, \( g(k_1, k_2) \geq 0 \) as \( \psi(L_a(k_1)) \leq L_b(k_2-1) \). We get \( g(k_1, k_2) \geq 0 \) with \( L_a(k_1) \geq L_b(k_2-1) \).

If \( L_a(k_1-1) < L_b(k_2) \), then \( g(k_1, k_2) = \psi(L_a(k_1) - L_b(k_2-1)) - \psi(L_a(k_1-1) - L_b(k_2-1)) \). We know that \( L_a(k_1) - L_b(k_2-1) > L_a(k_1-1) - L_b(k_2-1) > 0 \). Thus, \( g(k_1, k_2) > 0 \) as \( \psi(0) = 0 \).

Therefore, in this case \( g(k_1, k_2) > 0 \).

Case 3: \( L_a(k_1) \geq L_b(k_2) \)

In this case, \( L_a(k_1) > L_b(k_2-1) \) as \( L_b(k_2) > L_b(k_2-1) \). We distinguish three subcases: 1) \( L_a(k_1-1) < L_b(k_2-1) \), 2) \( L_a(k_1-1) < L_b(k_2) \) and \( L_a(k_1-1) \geq L_b(k_2-1) \), and 3) \( L_a(k_1-1) \geq L_b(k_2) \).

Subcase 1):

If \( L_a(k_1-1) < L_b(k_2-1) \), then

\[
g(k_1, k_2) = f(L_a(k_1), L_b(k_2-1)) - f(L_a(k_1), L_b(k_2)) \]

Since \( L_b(k_2-1) < L_b(k_2) \), we have \( L_a(k_1) - L_b(k_2-1) > L_a(k_1) - L_b(k_2) \). Thus, \( g(k_1, k_2) = 0 \) as \( \psi(0) = 0 \).

Subcase 2):

If \( L_a(k_1-1) < L_b(k_2) \) and \( L_a(k_1-1) \geq L_b(k_2-1) \), then \( g(k_1, k_2) \) takes the form shown in Equation [18], as \( L_a(k_1) \geq L_b(k_2) \).

\[
g(k_1, k_2) = \psi(L_a(k_1) - L_b(k_2)) - f(L_a(k_1), L_b(k_2)) \quad (18)
\]

Let \( L_a(k_1) - L_b(k_2) = \delta_1, L_a(k_2) - L_b(k_1-1) = \delta_2 \) and \( L_a(k_1-1) - L_b(k_2-1) = \delta_3 \), where \( \delta_1 \geq 0, \delta_2 > 0 \) and \( \delta_3 \geq 0 \).

Rewriting Equation [18] and substituting these values, we get the following expression,

\[
g(k_1, k_2) = \psi(L_a(k_1) - L_b(k_2)) - f(L_a(k_1), L_b(k_2)) \]

It can be verified that \( g(k_1, k_2) > 0 \) as \( \psi(\cdot) \) is convex.

Subcase 3):

If \( L_a(k_1-1) \geq L_b(k_2) \), then \( L_a(k_1) - L_b(k_2) > 0 \), \( L_a(k_1-1) - L_b(k_2-1) \geq 0 \), and \( L_a(k_1-1) - L_b(k_2) > 0 \). Hence,

\[
g(k_1, k_2) = \psi(L_a(k_1) - L_b(k_2)) - f(L_a(k_1), L_b(k_2)) \quad (18)
\]

In this subcase, let \( L_a(k_1) - L_a(k_1-1) = \delta_1, L_a(k_1-1) - L_b(k_2) = \delta_2 \) and \( L_a(k_1-1) - L_a(k_1-2) = \delta_3 \), where \( \delta_1 > 0 \), \( \delta_2 > 0 \) and \( \delta_3 > 0 \). Substituting this in the expression for \( g(k_1, k_2) \), we get

\[
g(k_1, k_2) = \psi(\delta_1 + \delta_2 + \delta_3) - \psi(\delta_2 + \delta_3) - \psi(\delta_1 + \delta_2) + \psi(\delta_2).
\]

Let us first consider the case, \( \delta_2 = 0 \), we get the following expression,

\[
g(k_1, k_2) = \psi(\delta_1 + \delta_3) - \psi(\delta_3) - \psi(\delta_1)
\]

It can be verified that \( g(k_1, k_2) > 0 \) as \( \psi(\cdot) \) is convex.

Next, consider the case when \( \delta_2 > 0 \). It can be observed that \( \delta_1 + \delta_2 + \delta_3 > \delta_1 + \delta_2 > \delta_2 \). Therefore, \( \delta_1 + \delta_2 \) can be expressed as,

\[
\delta_1 + \delta_2 = \lambda_1 \delta_2 + (1 - \lambda_1)(\delta_1 + \delta_2 + \delta_3)
\]

Solving for \( \lambda_1 \), we get \( \lambda_1 = \frac{\delta_1}{\delta_1 + \delta_3} \).

Similarly, it can be observed that \( \delta_1 + \delta_2 + \delta_3 > \delta_2 + \delta_3 > \delta_2 \) and \( \delta_2 + \delta_3 \) can be expressed as,

\[
\delta_2 + \delta_3 = \lambda_2 \delta_2 + (1 - \lambda_2)(\delta_1 + \delta_2 + \delta_3)
\]

where \( \lambda_2 = \frac{\delta_2}{\delta_1 + \delta_3} \).

From the definition of a convex function, and adding the above two expressions, we get the following,

\[
\psi(\delta_1 + \delta_2) + \psi(\delta_2 + \delta_3) \leq (\lambda_1 + \lambda_2)\psi(\delta_2) + (2 - \lambda_1 - \lambda_2)\psi(\delta_1 + \delta_2 + \delta_3).
\]

Substituting the value of \( \lambda_1 \) and \( \lambda_2 \), we get

\[
\psi(\delta_1 + \delta_2 + \psi(\delta_2 + \delta_3) \leq \psi(\delta_2) + \psi(\delta_1 + \delta_2 + \delta_3).
\]
Therefore it can be verified that \( g(k_1, k_2) \geq 0 \).

Thus, through these exhaustive cases, it is shown that for any \( k_1 \) and \( k_2 \), the function \( g(k_1, k_2) \geq 0 \) or in other words is non-negative.

**APPENDIX B**

**PROOF OF LEMMA 2**

**Lemma 2:** In any finite s-t cut \( C \), the total weight of the edges between any two adjacent columns \( a \) and \( b \) (denoted by \( C_{a,b} \)) equals to the surface smoothness cost of the resulting surface \( S_t \) with \( S_t(a) = k_1 \) and \( S_t(b) = k_2 \), which is \( \psi(L_a(k_1) - L_b(k_2)) \), where \( \psi(.) \) is a convex function.

**Proof:** Denote an edge from \( n_i(a, k_1) \) to node \( n_i(b, k_2) \) as \( E_i(a_{k_1}, b_{k_2}) \) for the \( i \)-th surface. Assume \( k_1 \geq k_2 \). Proof for the case when \( k_2 \geq k_1 \) can be done in a similar manner by interchanging the notations for column \( a \) and column \( b \).

To show: cost of cut \( C_{a,b} = \psi(L_a(k_1) - L_b(k_2)) \).

We start by observing such a s-t cut \( C_{a,b} \) will consist of only the following inter-column edges:

\[
\{ E_i(a_m, b_n) \mid 0 \leq m \leq k_1, \quad k_2 + 1 \leq n \leq L \}
\]

Note, here we use the index \( Z \) to denote the terminal node \( t \) as described in Section 2.2.2.

Summing up the weights of the above edges using Equation 6 we obtain the following expression:

\[
C_{a,b} = g(k_1, Z) + g(k_1, Z - 1) + g(k_1, Z - 2) + \ldots + g(k_1, k_2 + 1) \\
+ g(k_1 - 1, Z) + g(k_1 - 1, Z - 1) + g(k_1 - 1, Z - 2) + \ldots + g(k_1 - 1, k_2 + 1) \\
+ \ldots + g(0, Z) + g(0, Z - 1) + g(0, Z - 2) + \ldots + g(0, k_2 + 1)
\]

(19)

Let us first evaluate part of Equation 19 for \( k \), where \( 0 \leq k \leq k_1 \) as shown below:

\[
g(k, Z) + g(k, Z - 1) + g(k, Z - 2) + \ldots + g(k, k_2 + 1)
\]

where

\[
\begin{align*}
&= f(L_a(k), L_b(Z - 1)) - f(L_a(k), L_b(Z - 2)) - f(L_a(k), L_b(Z)), \\
&\quad - f(L_a(k), L_b(Z)) - f(L_a(k), L_b(Z)), \\
&\quad + f(L_a(k), L_b(Z - 2)) - f(L_a(k), L_b(Z - 1)) \\
&\quad + f(L_a(k), L_b(Z)) - f(L_a(k), L_b(Z - 1)) \\
&\quad - f(L_a(k), L_b(Z - 3)) + f(L_a(k), L_b(Z - 2)) \\
&\quad + f(L_a(k), L_b(Z - 2)) - f(L_a(k), L_b(Z - 1)) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), k_2 + 1) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), L_b(k_2)) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), k_2 + 1) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), L_b(k_2)) \\
&\quad = f(L_a(k), L_b(Z)) - f(L_a(k), L_b(Z)) \\
&\quad - f(L_a(k), L_b(Z)) + f(L_a(k), L_b(Z))
\end{align*}
\]

As described in Section 2.2.2.

\[
f(L_a(k), L_b(Z)) = 0, \quad f(L_a(k - 1), L_b(Z)) = 0 \quad (\because Z \notin z)
\]

(20)

By simplifying Equation 19 using Equation 20, it follows that:

\[
C_{a,b} = f(L_a(k_1), L_b(k_2)) - f(L_a(k_1), L_b(k_2)) - f(L_a(k_1 - 1), L_b(k_2)) \\
- f(L_a(k_1 - 1), L_b(k_2)) - f(L_a(k_1), L_b(k_2)) - f(L_a(k_1), L_b(k_2)) \\
+ f(L_a(k_1), L_b(k_2)) - f(L_a(k_1), L_b(k_2)) - f(L_a(k_1 - 1), L_b(k_2)) \\
+ f(L_a(k_1 - 1), L_b(k_2)) - f(L_a(k_1 - 1), L_b(k_2)) \\
= f(L_a(k_1), L_b(k_2)) - f(L_a(k_1 - 1), L_b(k_2)) \\
+ f(L_a(k_1 - 1), L_b(k_2)) - f(L_a(k_1 - 1), L_b(k_2))
\]

As described in Section 2.2.2.

\[
f(L_a(k_1), L_b(k_2)) = 0, \quad (\because -1 \notin z)
\]

(21)

Therefore, for this case it is shown that cost of cut \( C_{a,b} = \psi(L_a(k_1) - L_b(k_2)) \).

In a similar manner when \( k_2 \geq k_1 \), the s-t cut \( C_{b,a} \) will consist of the following inter-column edges:

\[
\{ E_i(b_m, a_n) \mid 0 \leq m \leq k_2, \quad k_1 + 1 \leq n \leq L \}
\]

Summing up the weights of the above edges using Equation 7 we obtain the following expression:

\[
C_{b,a} = g(k_2, Z) + g(k_2, Z - 1) + g(k_2, Z - 2) + \ldots + g(k_2, k_1 + 1) \\
+ g(k_2 - 1, Z) + g(k_2 - 1, Z - 1) + g(k_2 - 1, Z - 2) + \ldots + g(k_2 - 1, k_1 + 1) \\
+ \ldots + g(0, Z) + g(0, Z - 1) + g(0, Z - 2) + \ldots + g(0, k_1 + 1)
\]

(22)

Similar to the previous case, let us first evaluate part of Equation 22 for \( k \), where \( 0 \leq k \leq k_2 \) as shown below:

\[
g(k, Z) + g(k, Z - 1) + g(k, Z - 2) + \ldots + g(k, k_1 + 1)
\]

where

\[
\begin{align*}
&= f(L_a(k), L_a(Z - 1)) - f(L_a(k), L_a(Z - 2)) - f(L_a(k), L_a(Z)) \\
&\quad - f(L_a(k), L_a(Z)) - f(L_a(k), L_a(Z)), \\
&\quad + f(L_a(k), L_a(Z - 2)) - f(L_a(k), L_a(Z - 1)) \\
&\quad + f(L_a(k), L_a(Z)) - f(L_a(k), L_a(Z - 1)) \\
&\quad - f(L_a(k), L_a(Z - 3)) + f(L_a(k), L_a(Z - 2)) \\
&\quad + f(L_a(k), L_a(Z - 2)) - f(L_a(k), L_a(Z - 1)) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), k_2 + 1) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), L_b(k_2)) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), k_2 + 1) \\
&\quad - f(L_a(k), L_b(k_2)) - f(L_a(k), L_b(k_2)) \\
&\quad = f(L_a(k), L_a(Z)) - f(L_a(k), L_a(Z)) \\
&\quad - f(L_a(k), L_a(Z)) + f(L_a(k), L_a(Z))
\end{align*}
\]

(23)
\[ \psi(L_b(Z)) \]

This completes the proof.

\section*{References}

[1] K. Li, X. Wu, D. Chen, and M. Sonka, “Optimal surface segmentation in volumetric images—a graph-theoretic approach,” \textit{Pattern Analysis and Machine Intelligence, IEEE Transactions on}, vol. 28, no. 1, pp. 119–134, Jan 2006.

[2] M. D. Abràmoff, M. K. Garvin, and M. Sonka, “Retinal imaging and image analysis,” \textit{Biomedical Engineering, IEEE Reviews in}, vol. 3, pp. 169–208, 2010.

[3] D. J. Withey and Z. J. Koles, “A review of medical image segmentation: methods and available software,” \textit{International Journal of Bioelectromagnetism}, vol. 10, no. 3, pp. 125–148, 2008.

[4] Y. Yin, X. Zhang, R. Williams, X. Wu, D. D. Anderson, and M. Sonka, “Logismoslayered optimal graph image segmentation of multiple objects and surfaces: cartilage segmentation in the knee joint,” \textit{Medical Imaging, IEEE Transactions on}, vol. 29, no. 12, pp. 2023–2037, 2010.

[5] S. Kashyap, Y. Yin, and M. Sonka, “Automated analysis of cartilage morphology,” in \textit{Biomedical Imaging (ISBI), 2013 IEEE 10th International Symposium on}. IEEE, 2013, pp. 1300–1303.

[6] X. Wu, X. Dou, A. Wahle, and M. Sonka, “Region detection by minimizing intraclass variance with geometric constraints, global optimality, and efficient approximation,” \textit{Medical Imaging, IEEE Transactions on}, vol. 30, no. 3, pp. 814–827, 2011.

[7] H. Zhang, A. K. Abiose, D. Gupta, D. N. Campbell, J. B. Martins, M. Sonka, and A. Wahle, “Novel indices for left-ventricular dyssynchrony characterization based on highly automated segmentation from real-time 3-d echocardiography,” \textit{Ultrasound in medicine & biology}, vol. 39, no. 1, pp. 72–88, 2013.

[8] X. Liu, D. Z. Chen, M. H. Tawhai, X. Wu, E. A. Hoffman, and M. Sonka, “Optimal graph search based segmentation of airway tree double surfaces across bifurcations,” \textit{Medical Imaging, IEEE Transactions on}, vol. 32, no. 3, pp. 493–510, 2013.

[9] C. Bauer, M. A. Krueger, W. J. Lamm, B. J. Smith, R. W. Glenny, and R. R. Beichel, “Airway tree segmentation in serial block-face cryomicrotome images of rat lungs,” \textit{Biomedical Engineering, IEEE Transactions on}, vol. 61, no. 1, pp. 119–130, 2014.

[10] S. Sun, M. Sonka, and R. R. Beichel, “Lung segmentation refinement based on optimal surface finding utilizing a hybrid desktop/virtual reality user interface,” \textit{Computerized Medical Imaging and Graphics}, vol. 37, no. 1, pp. 15–27, 2013.

[11] X. Zhang, J. Tian, K. Deng, Y. Wu, and X. Li, “Automatic liver segmentation using a statistical shape model with optimal surface detection,” \textit{Biomedical Engineering, IEEE Transactions on}, vol. 57, no. 10, pp. 2622–2626, 2010.

[12] P. Song, Y. Liu, Y. Liu, P. K. Saha, M. Sonka, and X. Wu, “Graph search with appearance and shape information for 3-d prostate and bladder segmentation,” in \textit{Medical Image Computing and Computer-Assisted Intervention–MICCAI 2010}. Springer, 2010, pp. 172–180.

[13] M. K. Garvin, M. D. Abràmoff, X. Wu, S. R. Russell, T. L. Burns, and M. Sonka, “Automated 3-d intraretinal layer segmentation of macular spectral-domain optical coherence tomography images,” \textit{Medical Imaging, IEEE Transactions on}, vol. 28, no. 9, pp. 1436–1447, 2009.

[14] K. Lee, M. Niemeijer, M. K. Garvin, Y. H. Kwon, M. Sonka, and M. D. Abramoff, “Segmentation of the optic disc in 3-d oct scans of the optic nerve head,” \textit{Medical Imaging, IEEE Transactions on}, vol. 29, no. 1, pp. 159–168, 2010.

[15] Y. Cui, X. Wu, J. D. Newell, and M. Jacob, “Fat water decomposition using globally optimal surface estimation (goose) algorithm,” \textit{Magnetic Resonance in Medicine}, vol. 73, no. 3, pp. 1289–1299, 2015.

[16] H. Ishikawa, “Exact optimization for markov random fields with convex priors,” \textit{IEEE Transactions on Pattern Analysis and Machine Intelligence}, vol. 25, pp. 1333–1336, 2003.

[17] Y. Boykov, O. Veksler, and R. Zabih, “Fast approximate energy minimization via graph cuts,” \textit{Pattern Analysis and Machine Intelligence, IEEE Transactions on}, vol. 23, no. 11, pp. 1222–1239, Nov 2001.

[18] Y. Boykov and V. Kolmogorov, “An experimental comparison of min-cut/max-flow algorithms for energy minimization in vision,” \textit{Pattern Analysis and Machine Intelligence, IEEE Transactions on}, vol. 26, no. 9, pp. 1124–1137, 2004.

[19] Q. Song, J. Bai, M. K. Garvin, M. Sonka, J. M. Buatti, and X. Wu, “Optimal multiple surface segmentation with shape and context priors,” \textit{Medical Imaging, IEEE Transactions on}, vol. 32, no. 2, pp. 376–386, 2013.

[20] A. Shah, J. Bai, Z. Hu, S. Sadda, and X. Wu, “Multiple surface segmentation using truncated convex priors,” in \textit{Medical Image Computing and Computer-Assisted Intervention–MICCAI 2015}. Springer, 2015, pp. 97–104.

[21] X. Wu and D. Z. Chen, “Optimal net surface problems with applications,” in \textit{Automata, Languages and Programming}. Springer, 2002, pp. 1029–1042.

[22] P. A. Dufour, L. Cedrés, H. Abdillahi, S. Schroder, S. De Dzanet, U. Wolf-Schnurrbusch, and J. Kowal, “Graph-based multi-surface segmentation of oc data using trained hard and soft constraints,” \textit{Medical Imaging, IEEE Transactions on}, vol. 32, no. 3, pp. 531–543, 2013.

[23] M. P. Kumar, O. Veksler, and P. H. Torr, “Improved moves for truncated convex models,” \textit{J. Mach. Learn. Res.}, vol. 12, pp. 31–67, Feb. 2011.

[24] A. Shah, J.-K. Wang, M. K. Garvin, M. Sonka, and X. Wu, “Automated surface segmentation of internal limiting membrane in spectral-domain optical coherence tomography volumes with a deep cup using a 3-d range expansion approach,” in \textit{Biomedical Imaging (ISBI), 2014 IEEE 11th International Symposium on}. IEEE, 2014, pp. 1405–1408.

[25] M. D. Abràmoff, X. Wu, K. Lee, and L. Tang, “Subvoxel accurate graph search using non-euclidean graph space,” \textit{PloS one}, vol. 9, no. 10, p. e107763, 2014.

[26] F. Malmberg, J. Lindblad, N. Sladoje, and I. Nyström, “A graph-theoretic approach,” \textit{Pattern Analysis and Machine Intelligence, IEEE Transactions on}, vol. 9, no. 15, pp. 1338–1349, 2011.

[27] C. Shannon, “Communication in the presence of noise,” \textit{Proceedings of the IRE}, vol. 37, no. 1, pp. 10–21, Jan 1949.

[28] A. Trujillo-Pino, K. Krissanij, M. Alemán-Flores, and D. Santanacedrés, “Accurate subpixel edge location based on partial area effect,” \textit{Image and Vision Computing}, vol. 31, no. 1, pp. 72–90, 2013.
[29] M. Soret, S. L. Bacharach, and I. Buvat, “Partial-volume effect in pet tumor imaging,” Journal of Nuclear Medicine, vol. 48, no. 6, pp. 932–945, 2007.

[30] S. Farsiu, S. J. Chiu, R. V. O’Connell, F. A. Folgar, E. Yuan, J. A. Izatt, and C. A. Toth, “Quantitative classification of eyes with and without intermediate age-related macular degeneration using optical coherence tomography,” Ophthalmology, vol. 121, no. 1, pp. 162–172, 2014.

[31] C. Xu and J. L. Prince, “Snakes, shapes, and gradient vector flow,” Image Processing, IEEE Transactions on, vol. 7, no. 3, pp. 359–369, 1998.

[32] L. Breiman, “Random forests,” Machine learning, vol. 45, no. 1, pp. 5–32, 2001.

[33] J. Frostegård, “Sle, atherosclerosis and cardiovascular disease,” Journal of internal medicine, vol. 257, no. 6, pp. 485–495, 2005.

[34] S. Glagov, E. Weisenberg, C. K. Zarins, R. Stankunavicius, and G. J. Kolettis, “Compensatory enlargement of human atherosclerotic coronary arteries,” New England Journal of Medicine, vol. 316, no. 22, pp. 1371–1375, 1987.

[35] S. Balocco, C. Gatta, F. Ciompi, A. Wahle, P. Radeva, S. Carlier, G. Unal, E. Sanidas, J. Mauri, X. Carillo et al., “Standardized evaluation methodology and reference database for evaluating ivus image segmentation,” Computerized Medical Imaging and Graphics, vol. 38, no. 2, pp. 70–90, 2014.

[36] G. Unal, S. Bucher, S. Carlier, G. Slabaugh, T. Fang, and K. Tanaka, “Shape-driven segmentation of the arterial wall in intravascular ultrasound images,” Information Technology in Biomedicine, IEEE Transactions on, vol. 12, no. 3, pp. 335–347, 2008.

[37] V. Caselles, R. Kimmel, and G. Sapiro, “Geodesic active contours,” International journal of computer vision, vol. 22, no. 1, pp. 61–79, 1997.

[38] M.-H. R. Cardinal, J. Meunier, G. Soulez, R. L. Maurice, É. Therasse, and G. Cloutier, “Intravascular ultrasound image segmentation: a three-dimensional fast-marching method based on gray level distributions,” IEEE transactions on medical imaging, vol. 25, no. 5, pp. 590–601, 2006.

[39] M.-H. R. Cardinal, G. Soulez, J.-C. Tardif, J. Meunier, and G. Cloutier, “Fast-marching segmentation of three-dimensional intravascular ultrasound images: a pre-and post-intervention study,” Medical physics, vol. 37, no. 7, pp. 3633–3647, 2010.

[40] R. Downe, A. Wahle, T. Kovarnik, H. Skalicka, J. Lopez, J. Horak, and M. Sonka, “Segmentation of intravascular ultrasound images using graph search and a novel cost function,” in Proc. 2nd MICCAI workshop on computer vision for intravascular and intracardiac imaging, 2008, pp. 71–9.

[41] C. Gatta, E. Puertas, and O. Pujol, “Multi-scale stacked sequential learning,” Pattern Recognition, vol. 44, no. 10, pp. 2414–2426, 2011.

[42] F. Ciompi, O. Pujol, C. Gatta, M. Alberti, S. Balocco, X. Carrillo, J. Mauri-Ferre, and P. Radeva, “Holimab: A holistic approach for media–adventitia border detection in intravascular ultrasound,” Medical image analysis, vol. 16, no. 6, pp. 1085–1100, 2012.

[43] E. G. Mendizabal-Ruiz, M. Rivera, and I. A. Kakadiaris, “Segmentation of the luminal border in intravascular ultrasound b-mode images using a probabilistic approach,” Medical image analysis, vol. 17, no. 6, pp. 649–670, 2013.

[44] C. V. Bourantas, F. G. Kalatzis, M. I. Papafaklis, D. I. Fotiadis, A. C. Tweddell, I. C. Kourtis, C. S. Katsouras, and L. K. Michalis, “Angiocare: An automated system for fast three-dimensional coronary reconstruction by integrating angiographic and intracoronary ultrasound data,” Catheterization and Cardiovascular Interventions, vol. 72, no. 2, pp. 166–175, 2008.

[45] T. Ojala, M. Pietikäinen, and T. Mäenpää, “Multiresolution grayscale and rotation invariant texture classification with local binary patterns,” Pattern Analysis and Machine Intelligence, IEEE Transactions on, vol. 24, no. 7, pp. 971–987, 2002.