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Optimal Procedure Planning and Guidance System for Peripheral Bronchoscopy

Jason D. Gibbs,

Broncus Medical, Inc., Mountain View, CA 94043 USA (jgibbs@broncus.com)

Michael W. Graham,

Google, Inc., Pittsburgh, PA 15206 USA (mikegraham@google.com)

Rebecca Bascom,

Department of Medicine, Penn State Hershey Medical Center, Hershey, PA 17033 USA
(rbascom@psu.edu)

Duane C. Cornish,

Johns Hopkins University Applied Physics Lab, Laurel, MD 20723 USA (cornish.du@gmail.com)

Rahul Khare, and

Sheikh Zayed Institute, Children's National Medical Center, Washington, DC 20010 USA
(rahul.vedic@gmail.com)

William E. Higgins [Fellow, IEEE]

Department of Electrical Engineering, Pennsylvania State University, University Park, PA 16802 USA (weh2@psu.edu)

Abstract

With the development of multidetector computed-tomography (MDCT) scanners and ultrathin bronchoscopes, the use of bronchoscopy for diagnosing peripheral lung-cancer nodules is becoming a viable option. The work flow for assessing lung cancer consists of two phases: 1) 3-D MDCT analysis and 2) live bronchoscopy. Unfortunately, the yield rates for peripheral bronchoscopy have been reported to be as low as 14%, and bronchoscopy performance varies considerably between physicians. Recently, proposed image-guided systems have shown promise for assisting with peripheral bronchoscopy. Yet, MDCT-based route planning to target sites has relied on tedious error-prone techniques. In addition, route planning tends not to incorporate known anatomical, device, and procedural constraints that impact a feasible route. Finally, existing systems do not effectively integrate MDCT-derived route information into the live guidance process. We propose a system that incorporates an automatic optimal route-planning method, which integrates known route constraints. Furthermore, our system offers a natural translation of the MDCT-based route plan into the live guidance strategy via MDCT/video data fusion. An image-based study demonstrates the route-planning method's functionality. Next, we present a prospective lung-cancer patient study in which our system achieved a successful navigation rate of

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Correspondence to: William E. Higgins.

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91% to target sites. Furthermore, when compared to a competing commercial system, our system enabled bronchoscopy over two airways deeper into the airway-tree periphery with a sample time that was nearly 2 min shorter on average. Finally, our system's ability to almost perfectly predict the depth of a bronchoscope's navigable route in advance represents a substantial benefit of optimal route planning.

Keywords

Bronchoscopy; chest imaging; computed tomography; image-guided intervention systems; lung cancer; procedure planning; surgical guidance; virtual reality

I. Introduction

The continued advances in multidetector computed-tomography (MDCT) scanners and bronchoscope technology offer much promise for improving the lung-cancer assessment process and in particular the practice of bronchoscopy in the lung periphery [1]–[4]. The current state-of-the-art work flow for assessing lung cancer consists of two phases: 1) analysis of a patient's 3-D MDCT chest scan and 2) bronchoscopy [3], [5], [6].

During MDCT analysis, the physician uses a computer display to scroll through 2-D axial-plane sections of the 3-D scan to identify diagnostic regions of interest (ROIs), such as suspicious nodules, lymph nodes, and bronchoalveolar lavage (BAL) sites. During the analysis, the physician also ascertains bronchoscopy navigation routes through the airway tree leading to each ROI. Given that a typical MDCT scan consists of several hundred 2-D sections, this manual process is tedious and error prone, with route-planning errors arising as early as a second-generation airway [7]. Along this line, four issues exacerbate route planning [5], [8]. First, a route generally traverses several airway generations beyond the trachea. Second, the airway tree continually bifurcates in essentially any 3-D direction as a route is traversed. Third, 2-D airway cross sections are usually obliquely oriented relative to the axial-plane 2-D MDCT sections. Thus, an airway's structure along its length is deceptive to interpret from 2-D sections. Finally, many ROIs have complex 3-D shape and are not visible within an airway. This makes it difficult to judge which nearby airway offers the best approach to an ROI. In fact, a recent study showed that route-planning accuracy using manual inspection deteriorated to 40% for generation-4 routes [9].

Next, during bronchoscopy, the physician navigates the bronchoscope through the airway tree and, toward the end of a route, performs final target localization. In standard practice, this requires the physician to correlate the mentally derived MDCT-based airway routes and the bronchoscope's live video stream. Unfortunately, the bronchoscopic video, which depicts local endoluminal (interior) airway structure, and the MDCT scan, which gives 2-D cross-sectional images, bear no resemblance to each other. Thus, mentally defining the 3-D relationships between the bronchoscopic video, MDCT-derived airway routes, and target ROIs is difficult. In addition, since a target frequently lies outside the airways, hence being invisible to the bronchoscope, final target localization at the end of a route often must be done blindly [10], [11]. Along this line, previous research has shown a high degree of variability in bronchoscopy performance between physicians [10], [12]–[14]. Furthermore, a

recent peripheral bronchoscopy study reported a 78% navigation rate to the correct terminal airway leading to an ROI but only a 43% final ROI localization and sampling rate [14]. Fluoroscopy, CT fluoroscopy, and endobronchial ultrasound provide assistance for target confirmation or localization, but give limited guidance for bronchoscope navigation to the periphery and offer no direct link to the preprocedure MDCT scan [15], [16].

Recently, proposed image-guided bronchoscope-navigation systems offer a helpful bridge from MDCT analysis to live bronchoscopy [8], [16]–[25]. In particular, all of these systems link the preprocedure MDCT scan and live bronchoscopic video via MDCT-based virtual bronchoscopy (VB) [2], [10], [18], [24]. VB involves deriving simulated endoluminal airway views, or VB views, along an airway. A sequence of VB views provides a 3-D road map through the MDCT-derived “virtual” airways resembling the video stream provided by “real” videobronchoscopy. Early efforts highlighted VB’s potential for central-chest lymph-node biopsy [10], [11]. It has also been established that the endoluminal structure depicted in VB views correlates well with the structure seen in bronchoscopic video [17], [18], [26], [27]. A few systems employ electromagnetic guidance, which unfortunately involves extra hardware and does not provide direct bronchoscopic vision during navigation and localization [16], [19], [20]. The latter factor makes such systems susceptible to producing pneumothoraces. Another system proposes a hybrid approach incorporating electromagnetic guidance and image-based guidance, but has not been applied to humans [21].

Other purely image-based systems, which have been used for peripheral bronchoscopy, are simpler, requiring no elaborate sensor hardware [8], [22]–[24]. Furthermore, since the physician maneuvers the bronchoscope itself to a target, they enable direct vision of the entire route during navigation. While promising, these systems demand substantial route-planning time and draw upon error-prone interactive techniques. In addition, they offer no direct link between the MDCT-based route plan and live bronchoscopic video, nor do they offer data fusion between the MDCT-based VB space and bronchoscope video space. (A few systems are not sufficiently practical for live interactive human procedures [17], [25].)

On another front, recently proposed automated 3-D MDCT-analysis techniques, such as 3-D airway-tree segmentation and airway-centerline definition, can assist with route planning [28]–[33]. The airway-tree segmentation gives a 3-D airway-tree model and its endoluminal surfaces, while the centerlines define paths through the airways. Using these methods in tandem with 3-D computer graphics, complete 3-D routes can be interactively selected for an ROI. This approach solves the first three issues alluded to earlier. Unfortunately, ROI complexity makes this ad hoc approach suboptimal and can result in incorrect routes, as illustrated in Fig. 1. In addition, choosing a suitable route is daunting, as a typical 3-D chest scan produces over 100 distinct paths through the major airways.

Furthermore, known real constraints imposed by the bronchoscope and a particular procedure are not used during route planning. In addition, the route plan is insufficiently translated into the guidance system during a live procedure. For example, to perform a peripheral nodule biopsy, a viable airway route must be able to accommodate a specific bronchoscope and enable sufficient maneuverability along the entire route. Also, a guidance

system should interactively provide MDCT-derived route-planning information that facilitates effective navigation and final ROI localization for tissue biopsy.

The field of robotics has focused much attention on the route planning problem [34]. This has motivated research in bronchoscopy route planning, whereby device movements are computed to reach a goal site within an airway tree model [35]. While this paper uses device parameters, such as diameter and needle length, it does not link a plan directly to a 3-D chest scan, requires *a priori* knowledge of the final destination, and offers no guidance for ROI localization. Other efforts have required interactive route generation and knowledge of start/end points [36]. Finally, another semiautomatic MDCT-based planning method required a skilled user to manually specify a route's beginning and destination points and did not draw upon device or procedural constraints [24]. Thus, no method finds optimal routes to precisely defined ROIs in volumetric MDCT chest scans, while accounting for known physical constraints. Furthermore, no system integrates an MDCT-based route plan into a live bronchoscopy guidance strategy.

To their credit, Shinagawa *et al.* [22], [23] do comment on the need for greater automation in the planning process to make the system they tested more practical for routine peripheral bronchoscopy. They later briefly described on a rudimentary semiautomatic MDCT-based route-planning method (but gave no human study involving the method) [24]. The method used interactive manual thresholding to segment the airways and to define VB views. Also, it required a skilled physician or technician to manually specify a route's beginning and destination points, in addition to selecting a candidate route's final airway [24]. Notably, the method involves no use of device or procedural constraints and no notion of optimal route planning.

We present an optimal 3-D MDCT-based route-planning method that incorporates anatomical, device, and procedural constraints. We also describe a guidance system that offers a synergistic link between the MDCT-based route plan and subsequent live procedure. The system uses a seamless translation of MDCT-based route plan into the guidance strategy via MDCT/video data fusion. This effort constitutes part of a large bronchoscopy planning and guidance system under development by our group [30], [37]–[39].

Section II presents our optimal route-planning method and guidance system. Next, Section III demonstrates our route-planning method in an image-only study. It also presents an application of our system to an extensive peripheral-bronchoscopy patient study and benchmarks our system's results to those achieved in recent competing clinical studies. Finally, Sections IV and V discuss the results and offer final remarks.

II. Methods

Our system parallels the standard peripheral bronchoscopy work flow via two stages of interaction: 1) 3-D MDCT analysis; and 2) image-guided bronchoscopy (see Fig. 2). Given a patient's MDCT chest scan and a set of route constraints, 3-D MDCT analysis produces a route plan, consisting of a feasible bronchoscope navigation route for each ROI. Next, image-guided bronchoscopy occurs live in the bronchoscopy suite. Using a graphical user

interface coupled with MDCT/video data fusion, our system gives the physician real-time feedback during bronchoscope navigation and final ROI localization.

Sections II-A and II-B describe 3-D MDCT analysis with a particular emphasis on optimal route planning. Next, Section II-C details the system's usage during image-guided bronchoscopy, with a focus on how the computed route plan seamlessly integrates into the live guidance strategy via phased data fusion. Finally, Section II-D concludes with system implementation details.

A. 3-D MDCT Analysis and the Route-Planning Problem

We first summarize the 3-D MDCT analysis process followed by a detailed layout of the route-planning problem. Following the standard protocol for lung-cancer patients, we draw upon high-resolution 3-D MDCT chest volumes I having spatial resolution on the order of 0.5–1.0 mm in the x -, y -, and z -dimensions, with a typical volume I consisting of ≈ 500 2-D transverse-plane sections [1], [30]. Each voxel $\mathbf{x}$ at location (x, y, z) in I has a brightness value $I(x, y, z)$ given in Hounsfield units (HU) nominally over the calibrated range $[-1000$ HU, 1000 HU] [40].

As per Fig. 2(a), 3-D MDCT analysis begins with the physician defining target ROIs $\mathbf{R}_k$, $k = 1, 2, \dots, K$, in I , where each ROI is represented by its constituent voxels in I . For our studies, we either employed the interactive live-wire mechanism to define an ROI or we placed a small sphere to designate a BAL, brush, or airway exam location [see Fig. 3(a)] [41]. Next, a series of automatic operations produce a patient-specific airway-tree model from I . To this end, airway-tree segmentation followed by surface definition define the segmented 3-D airway tree along with associated endoluminal airway surfaces I_S [6], [28]–[30], [37]. Next, centerline calculation and geometric-measurement computation give the central axes along the airways captured by I_S [see Fig. 3(b)] [42]. Finally, automatic route planning computes a series of optimal endobronchial routes leading to each target ROI [see Fig. 3(c)].

All operations employed for ROI definition and airway-tree model calculation have been previously developed and undergone extensive validation with human data [6], [28]–[30], [37], [42]. We now give a detailed layout of the route-planning problem, which has not been described previously. Section II-B then discusses our methods for optimal route planning.

Paralleling conventions in Swift *et al.* and Kiraly *et al.*, let the centerlines of the airway tree I_S comprise a tree structure $\mathbf{T} = (\mathbf{V}, \mathbf{B}, \mathbf{P})$, where $\mathbf{V} = \{\mathbf{v}_1, \mathbf{v}_2, \dots, \mathbf{v}_L\}$ is the set of view sites, $\mathbf{B} = \{\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_M\}$ is the set of branches, $\mathbf{P} = \{\mathbf{p}_1, \mathbf{p}_2, \dots, \mathbf{p}_N\}$ is the set of paths, and L , M , and N are integers ≥ 1 [29], [33]. A view site $\mathbf{v}_I = (\mathbf{x}_I, \mathbf{t}_I, \mathbf{u}_I, d_I, \theta_I)$ is the basic discrete element constituting the centerlines. By convention, the first view site $\mathbf{v}_1$ always denotes the tree's root site located in the trachea. Component $\mathbf{x}_I$ corresponds to $\mathbf{v}_I$'s 3-D location (x, y, z) . Unit vectors $\mathbf{t}_I$ and $\mathbf{u}_I$ define the navigation directions about $\mathbf{x}_I$. Vector $\mathbf{t}_I$ points toward the viewing direction tangential to the centerline, while $\mathbf{u}_I$ is the up vector specifying viewing orientation and lies perpendicular to the centerline. A view site $\mathbf{v}_I$ can connect to other successor (child) view sites in three ways: 1) connect to a unique successor—i.e., $\mathbf{v}_I$ occurs within the interior of a branch; 2) connect to two view sites—i.e., $\mathbf{v}_I$ is a bifurcation point; and 3) connect to no successor view sites i.e., $\mathbf{v}_I$ is a branch endpoint.

Each view site $\mathbf{v}_l$ also includes the minimum lumen diameter (minor axis length) d_l and branch angle θ_l . While airways are thin tubular structures, they generally do not have circular cross sections. To account for this, d_l characterizes an airway's narrowest extent within the 2-D cross section perpendicular to view site $\mathbf{v}_l$. The branch angle θ_l equals the angle formed between the line segments connecting $\mathbf{v}_{l-1}$, $\mathbf{v}_l$, and $\mathbf{v}_{l+1}$; i.e.,

$\theta_l = \cos^{-1}[\langle \overline{\mathbf{x}_{l-1}\mathbf{x}_l}, \overline{\mathbf{x}_l\mathbf{x}_{l+1}} \rangle]$, where $\langle a, b \rangle$ signifies the normalized dot product of its arguments a and b . Root site $\mathbf{v}_1$ has $\theta_1 = 0$ by default. Typically, branch angles are near zero for view sites within a branch's interior and take on large values near bifurcation points.

A branch $\mathbf{b}_m$ consists of an ordered set of ω_m connected view sites

$$\mathbf{b}_m = \{\mathbf{v}_{m,1}, \mathbf{v}_{m,2}, \dots, \mathbf{v}_{m,\omega_m}\}, \quad (1)$$

where $\mathbf{v}_{m,1}, \dots, \mathbf{v}_{m,\omega_m} \in \mathbf{V}$. View sites $\mathbf{v}_{m,1}$ and $\mathbf{v}_{m,\omega_m}$ terminating $\mathbf{b}_m$ must be either a bifurcation point or an endpoint. Branch $\mathbf{b}_1$ always denotes the tree's root branch (the trachea), where $\mathbf{b}_1$'s first view site $\mathbf{v}_{1,1} = \mathbf{v}_1$, the root site. Branch $\mathbf{b}_m$ is a terminal airway if it concludes with a branch endpoint. A path

$$\mathbf{p}_n = \{\mathbf{b}_1, \mathbf{b}_{n,2}, \mathbf{b}_{n,3}, \dots, \mathbf{b}_{n,\omega_n}\}, \quad (2)$$

consists of an ordered set of ω_n connected branches $\mathbf{b}_1, \mathbf{b}_{n,2}, \dots \in \mathbf{B}$. Note that the last view site of $\mathbf{b}_{n,2}$ equals the first view site of $\mathbf{b}_{n,3}$, or $\mathbf{v}_{(n,2),\omega_{(n,2)}} = \mathbf{v}_{(n,3),1}$ per (1) and (2), etc. Clearly, such a view site is a bifurcation point. As per (2), all paths begin with the root branch $\mathbf{b}_1$ and end at some terminal airway $\mathbf{b}_{n,\omega_n}$. In addition, a unique path exists in $\mathbf{P}$ for each of the tree's terminal airways. Thus, the path set $\mathbf{P}$ contains all potential navigable routes through the airway tree leading to a terminal airway.

Note that a route leading to ROI $\mathbf{R}_k$ in general does not terminate at the end of an airway. Therefore, we require a separate data structure to represent a route leading to $\mathbf{R}_k$:

$$\mathbf{r}_k = \{\mathbf{v}_1, \mathbf{v}_{k,2}, \mathbf{v}_{k,3}, \dots, \mathbf{v}_{D_k}\}, \quad (3)$$

where $\mathbf{r}_k$ consists of an ordered set of connected view sites. The final site $\mathbf{v}_{D_k}$ denotes the route destination, generally located near $\mathbf{R}_k$. As per (3), to enable bronchoscopic navigation, every feasible route $\mathbf{r}_k$ starts in the trachea and, hence, must start at the tree's root site $\mathbf{v}_1$. In addition, just as each of the tree's terminal airways has one and only one path leading to it, there is also one and only one optimal route $\mathbf{r}_k$ leading to $\mathbf{R}_k$, given a set of constraints. Finally, note that a route is actually a partial path; i.e., $\exists \mathbf{p}_n \in \mathbf{P}$ such that $\mathbf{r}_k \subset \mathbf{p}_n$. Thus, the ordered sequence of view sites (3) constituting $\mathbf{r}_k$ is unique.

B. Optimal Route Planning

A feasible route $\mathbf{r}_k$ leading to each ROI $\mathbf{R}_k$ must meet all known constraints to enable successful bronchoscope navigation and ROI localization. For clarity, we will drop the

subscript k and consider a route $\mathbf{r}$ associated with an ROI $\mathbf{R}$. Three classes of constraints influence which routes are feasible.

1. Anatomical—The 3-D airway-tree defines the navigation environment. The previously defined airway-tree model provides this information through the following quantities:
 - a. Global tree structure $\mathbf{T} = (\mathbf{V}, \mathbf{B}, \mathbf{P})$, airway-tree surfaces I_S , and raw image I
 - b. Local geometrical characteristics associated with each view site $\mathbf{v}_l \in \mathbf{V}$:
 - i. minimum lumen diameter d_l (units = mm),
 - ii. branch angle θ_l (units = degrees).
2. Device—The bronchoscope's physical characteristics and mechanical properties define its maneuverability within the tree. The following parameters, readily available as part of the published information provided by manufacturers, specify the bronchoscope's characteristics:
 - a. diameter d_B (units = mm),
 - b. maximum bending angle θ_B , where θ_B indicates the maximum angle that the bronchoscope's tip can be articulated (units = degrees),
 - c. minimum diagnostic field-of-view (FOV) angle θ_{FOV} (units = degrees).
3. Procedural—These factors impose conditions on the ability to perform desired tasks. The following parameters specify the conditions we consider:
 - a. Maximum allowed distance n_L of final route destination $\mathbf{v}_D$ from an ROI $\mathbf{R}$ (units = mm).
 - b. Proper navigation directions $(\mathbf{t}_l, \mathbf{u}_l)$ for all view sites $\mathbf{v}_l$ on a route.

Below, we elaborate more fully on these constraints and how they interact to produce specific route restrictions. We then give a series of computationally efficient algorithms for deriving optimal routes.

Fundamentally, the bronchoscope must be navigable along an entire route toward an ROI; i.e., it must be able to fit within the airway tree at all view sites of a route and it must be maneuverable through all turns encountered along a route. This brings about two restrictions on navigable view sites $\mathbf{v}_l$:

$$d_B < d_l \quad (4)$$

$$\theta_B > \theta_l. \quad (5)$$

In other words, $\forall \mathbf{v}_I \in \mathbf{r}$, (4) states that the bronchoscope must be able to fit within the airway lumen associated with view site $\mathbf{v}_I$, while (5) states that the bronchoscope must have sufficient flexibility to bend through the lumen at $\mathbf{v}_I$ [see Fig. 4(a)].

Next, when near ROI $\mathbf{R}$'s vicinity, the physician must be able to perform target localization and the desired diagnostic task. Stated differently, the physician demands a bronchoscopic video field of view (FOV) that enables proper examination and maneuverability. This imposes conditions on route destination $\mathbf{v}_D$. For the 40% of peripheral ROIs that are endoluminal—i.e., those that appear in the airway or impinge on the airway—a “head on” $\approx 0^\circ$ approach enables procedure completion (e.g., a needle can pierce the ROI). For extraluminal ROIs, however, many candidate route destinations may be impractical; in the worst case, no feasible route may exist. When near an extraluminal ROI's vicinity, a feasible route must satisfy two conditions: 1) it must be within the bronchoscope's FOV; 2) it must be sufficiently close to a navigable view site to enable the procedure completion.

These conditions can be captured by a bronchoscope's “diagnostic FOV,” defined as a cone originating at $\mathbf{x}_D$ and oriented along viewing direction $\mathbf{t}_D$ [see Fig. 4(b)]. The cone's solid angle coverage is determined by θ_{FOV} , while its height (depth) is specified by n_L . Thus, a feasible route destination $\mathbf{v}_D$ is one where $\mathbf{R}$ is visible within the cone and sufficiently close to $\mathbf{v}_D$; i.e., $\mathbf{R}$ impinges on the cone. These considerations lead to two restrictions on a feasible destination $\mathbf{v}_D$: i.e., if $\exists \mathbf{x} \in \mathbf{R}$ such that $\|\mathbf{x}_D - \mathbf{x}\| \leq n_L$ or

$$\|\mathbf{x}_D - \partial\mathbf{R}\| \leq n_L \quad (6)$$

$$\theta_{\mathbf{x}} < \theta_{\text{FOV}} \quad (7)$$

where $\mathbf{R}$ represents the exterior surface (boundary) of $\mathbf{R}$, and

$$\theta_{\mathbf{x}} = \cos^{-1}[\langle \mathbf{x} - \mathbf{x}_D, \mathbf{t}_D \rangle]. \quad (8)$$

Restriction (6) states that the ROI must impinge on the diagnostic FOV. If the desired task is a needle biopsy, n_L is typically set to reflect the needle length; i.e., the needle can extend at least a distance n_L mm from the bronchoscope's tip. Thus, to perform a feasible needle biopsy, the distance from where the needle punctures the airway wall to ROI $\mathbf{R}$ must be $< n_L$ mm to acquire a tissue sample. If instead the bronchoscopic procedure involves a lavage, brushing, or airway examination, then $n_L = 0$ in (6), as the requirement now is to reach the location. Restriction (7) states that at least one voxel constituting the ROI must be visible near the final route destination; this is equivalent to requiring at least one ROI surface voxel $\mathbf{x} \in \mathbf{R}$ be visible. In reality, however, because θ_{FOV} is generally picked conservatively (see Section III), a significant fraction of $\mathbf{R}$ will tend to be visible near $\mathbf{v}_D$.

Finally, in general practice, the physician employs a standard method for orienting the bronchoscope along a route to enable logical, intuitive navigation. This requires that all view sites $\mathbf{v}_l$ constituting a route incorporate proper navigation directions $(\mathbf{t}_l, \mathbf{u}_l)$. Note that the physician can freely rotate the bronchoscope's FOV during navigation by twisting the device. In fact, following general practice, the physician applies three tenets when rotating and advancing the bronchoscope [44].

1. The bronchoscope faces a visible branch bifurcation.
2. Each successive child airway of a route appears in the top ("Up") part of the bronchoscope's FOV.
3. The target ROI occupies the center of the FOV during final target localization.

Recall that the MDCT-based centerlines give navigation directions $(\mathbf{t}_l, \mathbf{u}_l)$ associated with each $\mathbf{v}_l$. Unfortunately, the centerlines do not correspond to FOV orientations desired for bronchoscope navigation. In addition, the available directions bear no relation to the desired FOV for final ROI localization.

To produce new navigation directions, our method accounts for the three bronchoscopy tenets listed above. Directions are computed so that each view site faces the end of its constituent branch. Also, view sites approaching a branch end are modified so that each child branch appears up in the bronchoscope FOV. For localization, view sites near $\mathbf{v}_D$ are modified so that the ROI appears centered in the bronchoscope FOV. Finally, directions are found so that branch-to-branch transitions and on the final target approach are smooth and reflective of how the real device rolls through the airways.

To help describe our method, assume without loss of generality that route $\mathbf{r}$ for ROI $\mathbf{R}$ consists of Q view sites and arises from a path $\mathbf{p} \in \mathbf{P}$ such that $\mathbf{r} \subset \mathbf{p}$. Furthermore, assume $\mathbf{r}$ consists of the first a branches constituting $\mathbf{p}$ and a portion of $\mathbf{p}$'s $(a + 1)$ th branch. Thus, we consider the following:

$$\mathbf{r} = \{\mathbf{v}_1, \mathbf{v}_2, \mathbf{v}_3, \dots, \mathbf{v}_{Q-1}, \mathbf{v}_Q\} \quad (9)$$

$$= \{\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_{a-1}, \mathbf{b}_a, \mathbf{v}_{a+1,1}, \mathbf{v}_{a+1,2}, \dots, \mathbf{v}_Q\} \quad (10)$$

$$= \{\mathbf{b}_1, \mathbf{b}_2, \dots, \mathbf{b}_{a-1}, \mathbf{v}_{a,1}, \mathbf{v}_{a,2}, \dots, \mathbf{v}_{a,\omega_a}, \mathbf{v}_{a+1,2}, \dots, \mathbf{v}_D\} \quad (11)$$

where the Q th view site $\mathbf{v}_Q$ is the route destination $\mathbf{v}_D$, $\mathbf{v}_1$ is the root site, $\mathbf{b}_1$ is the root branch, and $\mathbf{b}_m$, $m > 1$, represents the m th branch constituting $\mathbf{r}$. In addition, $\mathbf{v}_{m,l}$ denotes the l th view site of branch $\mathbf{b}_m$ per (1). Finally, notice in (10) and (11) that $\mathbf{v}_{a+1,1}$ and $\mathbf{v}_{a,\omega_a}$ represent the same view site and equal the bifurcation point linking branches $\mathbf{b}_a$ and $\mathbf{b}_{a+1}$.

We derive new tangent vector $\mathbf{t}_{m,l}$ for view site $\mathbf{v}_{m,l}$ using

$$\mathbf{t}_{m,l} = \frac{\mathbf{x}_{m,\omega_m} - \mathbf{x}_{m,l}}{\|\mathbf{x}_{m,\omega_m} - \mathbf{x}_{m,l}\|} \quad (12)$$

which results in the bronchoscope FOV at $\mathbf{v}_{m,l}$ pointing toward the end of branch $\mathbf{b}_m$. To avoid abrupt directional changes near bifurcation points, we modify $\mathbf{t}_{m,l}$ by blending $\mathbf{t}_{m,l}$ with the tangent vector of its parent branch's endpoint $\mathbf{t}_{m-1,\omega_{m-1}} = \mathbf{t}_{m,1}$, using the method of [29]. Only the first $(\lambda - 1)$ view sites undergo this blending, as the influence of $\mathbf{v}_{m,1}$ diminishes for increasing l .

To maintain smooth navigation, we also compute new up vectors. To do this, we project the previous view site's up vector onto the current view site's FOV viewing plane, where the plane for $\mathbf{v}_{m,l}$ is defined by FOV center $\mathbf{x}_{m,l}$ and tangent vector $\mathbf{t}_{m,l}$ [45]. This process maintains the essential constraint that an up vector must be orthogonal to its corresponding tangent vector. Because we require child branch $\mathbf{b}_{m+1}$ to appear in the top of the FOV as the bronchoscope approaches branch end $\mathbf{b}_m$, we include a second modification for view sites near a branch end; i.e., to have child branch $\mathbf{b}_{m+1}$ appear in the top of the FOV, the up vector for $\mathbf{v}_{m,\omega_m} = \mathbf{v}_{m+1,1}$ is constrained to be

$$\mathbf{u}_{m,\omega_m} = -((\mathbf{t}_{m,1} \times \mathbf{t}_{m+1,1}) \times \mathbf{t}_{m,1}) \quad (13)$$

where “ $\times$ ” signifies vector cross product and $\mathbf{t}_{m,1}$ and $\mathbf{t}_{m+1,1}$ are newly blended tangent vectors oriented at the first view sites on their respective branches and pointing toward the last view sites on their branches. Eq. (13) projects child branch $\mathbf{b}_{m+1}$'s direction $\mathbf{t}_{m+1,1}$ onto the FOV plane of parent branch $\mathbf{b}_m$'s final view site. As a final step, for a branch $\mathbf{b}_m$'s last λ view sites—i.e., those view sites approaching the next branch endpoint, the up vectors undergo a blending with $\mathbf{u}_{m,\omega_m}$ of (13), similar to the blending that produces the new tangent vectors, to make branch-to-branch transitions smooth.

Lastly, for view sites near the ROI, we project the direction vector $\mathbf{t}_R$ at $\mathbf{v}_D$ pointing toward ROI $\mathbf{R}$'s centroid onto destination view site $\mathbf{v}_D$'s FOV plane; i.e., $\mathbf{t}_R$ serves as the final child up vector in (13) for branch $\mathbf{b}_{d+1}$ to give $\mathbf{u}_D$. Up vector $\mathbf{u}_D$ is then blended with the final λ view sites of the route.

Given the discussion above, the optimal route planning problem therefore entails finding for each ROI $\mathbf{R}_k$, $k = 1, 2, \dots, K$, a feasible route $\mathbf{r}_k$ that satisfies all restrictions (4–8) and has suitable navigation directions using (12–13), consistent with the given anatomical, device, and procedural constraints. We designate the optimal route $\mathbf{r}$ as the one that allows the closest approach to $\mathbf{R}$; i.e., $\mathbf{r}$ minimizes the distance between the destination $\mathbf{v}_D$ and the surface of $\mathbf{R}$ over the set of all feasible candidate destinations.

Algorithms 1 and 2 give our methods for performing optimal route planning for a given ROI. Algorithm 1 takes as inputs the tree structure, airway-tree surfaces, ROI, and constraints, and outputs a route consistent with the various constraints. Algorithm 2 then computes procedure-specific directions to give the final optimal route. Each route $\mathbf{r}$ consists of a

connected set of view sites originating from the root site $\mathbf{r}_1$ and terminating at a destination site $\mathbf{v}_D$ that points toward ROI $\mathbf{R}$'s centroid. Note that $\mathbf{r}$ need not reach $\mathbf{R}$'s surface, such as in the case for extraluminal ROIs. Yet, as shown in Section III, Algorithms 1 and 2 can point out situations where the desired bronchoscope procedure cannot be performed; e.g., no valid route exists that satisfies the given constraints to enable a successful needle biopsy.

Algorithm 1 begins with a depth-first search for view sites $\mathbf{v}_{m,l}$ that permit navigation of the specified bronchoscope through the airway tree (lines 4–13). If $\mathbf{v}_{m,l}$ fails either test (4) and (5) (line 6), then it corresponds to a constriction; i.e., a location where the bronchoscope cannot be navigated. Thus, per line 9, $\mathbf{v}_{m,l}$ and the entire subtree succeeding it, including all view sites and branches in addition to all paths ending at sites within the subtree, are pruned. A second search focusing on the localization phase next examines the pruned tree to find the route destination satisfying restrictions (6) and (7) and achieving the minimum Euclidean distance to the ROI's surface (lines 14–32). A view site $\mathbf{v}_{m,l}$ with $d = 0$ implies that the ROI is within the airway at this location—the search can be terminated immediately. At line 17, only surface voxels $\mathbf{x} \in \mathbf{R}$ need to be considered, because at least one such voxel always exists that is closer than any given interior voxel of $\mathbf{R}$. At the conclusion, function **route**($\cdot$) delineates the computed route $\mathbf{r}$.

Algorithm 2 next takes the computed route ROI and tree structure as inputs to derive a modified route having the proper viewing directions. It begins by computing a new tangent vector for the root site, while retaining the up vector. For each subsequent view site, the algorithm computes the desired tangent and up vectors, with tangent-vector blending occurring for the λ view sites at the beginning of each branch and up-vector blending occurring for the λ view sites at the end of each branch. The **tangent**($\cdot$), **blend**($\cdot$), and **upChild**($\cdot$) functions use relations (12) and (13). The first part of Algorithm 2 focuses on computing new directions for the navigation phase (lines 7–13), while

Algorithm 1

Find closest feasible route $\mathbf{r}$ for ROI $\mathbf{R}$.

```

1: Inputs:
   tree structure  $\mathbf{T} = (\mathbf{V}, \mathbf{B}, \mathbf{P})$  and surfaces  $I_s$ 
   bronchoscope and procedural constraints
    $(d_B, \theta_B, \theta_{FOV}, n_L)$ 
   ROI  $\mathbf{R}$ 
2:  $\mathbf{T}_p \leftarrow \mathbf{T}$  // Initialize pruned tree
3: distance =  $\infty$ ;  $\mathbf{v}_D = \text{NULL}$ 
4: for all branches  $\mathbf{b}_m \in \mathbf{B}$  do
5:   for all view sites  $\mathbf{v}_{m,l} \in \mathbf{b}_m$  do
6:     if  $d_B < d_{m,l}$  and  $\theta_B > \theta_{m,l}$  then
7:       continue
8:     else
9:        $\mathbf{T}_p \leftarrow \text{prune}(\mathbf{T}_p, \mathbf{v}_{m,l})$ 
10:    goto 13

```

```

// Terminate examination of branch  $\mathbf{b}_m$ 
11:   end if
12:   end for
13: end for
14: for all branches  $\mathbf{b}_m \in \mathbf{B}_p$  do
15:   distancem =  $\infty$ ;  $\mathbf{v}_{Dm}$  = NULL
16:   for all view sites  $\mathbf{v}_{m,l} \in \mathbf{b}_m$  do
17:     for all voxels  $\mathbf{x} \in \mathbf{R}$  do
18:        $d = \|\mathbf{x} - \mathbf{x}_{m,l}\|$ 
19:        $\theta_x = \cos^{-1} [\langle \mathbf{x} - \mathbf{x}_{m,l}, \mathbf{t}_{m,l} \rangle]$  using (8)
20:       if  $d \leq n_l$  and  $\theta_x < \theta_{FOV}$  then
21:         if  $d < \text{distance}_m$  then
22:           distancem  $\leftarrow d$ 
23:            $\mathbf{v}_{Dm} \leftarrow \mathbf{v}_{m,l}$ 
24:         end if
25:       end if
26:     end for
27:   end for
28:   if distancem < distance then
29:     distance = distancem
30:      $\mathbf{v}_D = \mathbf{v}_{Dm}$ 
31:   end if
32: end for
33: return  $\mathbf{r} = \text{route}(\mathbf{v}_D, \mathbf{T}_p)$ 

```

the computation for the route's final λ sites is for the ROI localization phase (lines 14–17). With respect to lines 11 and 14, the algorithm assumes for clarity that $\mathbf{v}_{a+1}, \omega_{a+1} = \mathbf{v}_D$; it also assumes that the final λ view sites occur on the last $(a + 1)$ th branch of $\mathbf{r}$ (they could, of course, begin on an earlier branch).

To conclude optimal route planning, our system generates a prebronchoscopy report for each route, studied by the physician prior to bronchoscopy as discussed in Section II-C [see Fig. 2(b)].

Note that a typical 3-D MDCT chest scan gives a tree consisting of roughly $L = 5000$ view sites, $M = 200$ branches, and $N = 100$ unique paths. Hence, the size of tree structure $\mathbf{T}$ is such that the planning algorithms demand negligible computation time. In addition, the algorithms have essentially no parameters; all values arise from the constraints of the specific

Algorithm 2

Determine procedure-specific viewing directions for route found by Algorithm 1.

1: **Inputs:**

```

tree structure  $\mathbf{T} = (\mathbf{V}, \mathbf{B}, \mathbf{P})$ 
route  $\mathbf{r}$ , ROI  $\mathbf{R}$ 
2:  $\mathbf{t}_1 \leftarrow \text{tangent}(\mathbf{x}_{1,1}, \mathbf{x}_1, \omega_1)$  using (12)
3: Leave  $\mathbf{u}_1$  unchanged
4: for all branches  $\mathbf{b}_m, m = 1, 2, \dots, a + 1$  do
5:   for all view sites  $\mathbf{v}_{m,l}, l = 2, \dots, \omega_m$  do
6:      $\mathbf{t}_{m,l} \leftarrow \text{tangent}(\mathbf{x}_{m,l}, \mathbf{x}_m, \omega_m)$ 
7:     if  $\mathbf{v}_{m,l} < \lambda$  view sites
       from beginning of  $\mathbf{b}_m$  then
8:        $\mathbf{t}_{m,l} \leftarrow \text{blend}(\mathbf{t}_{m,1}, \mathbf{t}_{m,l})$ 
9:     end if
10:     $\mathbf{u}_{m,l} \leftarrow \text{project}(\mathbf{u}_{m,l-1}, \mathbf{v}_{m,l})$ 
11:    if  $\mathbf{v}_{m,l} < \lambda$  view sites from end of  $\mathbf{b}_m$  and
        $m < a + 1$  then
12:       $\mathbf{u}_c \leftarrow \text{upChild}(\mathbf{t}_{m,1}, \mathbf{t}_{m+1,1})$  using (13)
13:       $\mathbf{u}_{m,l} \leftarrow \text{blend}(\mathbf{u}_{m,l}, \mathbf{u}_c)$ 
14:    else if  $\mathbf{v}_{m,l} < \lambda$  view sites
       from destination  $\mathbf{v}_D$  then
15:       $\mathbf{d}_c \leftarrow \text{upChild}(\mathbf{t}_{a,1}, \mathbf{t}_R)$ 
16:       $\mathbf{u}_{m,l} \leftarrow \text{blend}(\mathbf{u}_{m,l}, \mathbf{d}_c)$ 
17:    end if
18:  end for
19: end for
20: return final optimal route  $\mathbf{r}$ 

```

clinical situation. Parameter λ used by Algorithm 2 does strictly speaking affect the view sites constituting the computed route. Its value dictates the smoothness of transitions along a route and depends on the resolution of the MDCT data. We use $\lambda = 9$ as a default, meaning that branch-to-branch transitions occurred over a 5–10 mm distance.

Regarding typical patient characteristics, peripheral airways 9 generations from the trachea typically have diameters $d_l > 3$ mm and branch angles $\theta_l < 90^\circ$. Also, an airway generally has a length > 10 mm, implying > 20 computed view sites per branch, where the view sites have a spacing on the order of the MDCT spatial resolution. Section III gives further quantitative data for typical patients and bronchoscopes. (As a side point, the Olympus BF-type MP160F ultrathin bronchoscope, the primary device used for peripheral bronchoscopies is the shortest device listed in Table I, with a length of 870 mm. Note, however, that this length is far more than sufficient to reach any peripheral airway in the human lungs. Hence, bronchoscope length need not be considered as a constraint.)

C. Image-Guided Bronchoscopy System

After completing 3-D MDCT Analysis, the next stage of interaction with our system is image-guided bronchoscopy [see Fig. 2(b)]. Two basic tasks occur here: 1) report inspection; and (2) live bronchoscopy.

During report inspection, the physician essentially performs a “virtual procedure” for each ROI, as suggested by the prebronchoscopy route report. Each report depicts the suggested route to navigate and consists of two parts: 1) a static single-page synopsis showing all bifurcation points; and 2) an interactive movie viewer [see Fig. 5(a)]. In our studies, the physician inspected the reports on a tablet PC offline while the bronchoscopy suite was being set up for the patient. The physician also often briefly reviewed a route’s report again on the guidance computer just before navigating the real bronchoscope. By studying the report’s visual and quantitative information, the physician essentially “rehearses” the bronchoscopy. This preview helps the physician foresee challenges such as tight turns and difficult airway maneuvers and helps imprint the route in the physician’s mind. Yu *et al.* [38] give complete detail on this task.

Before describing the live bronchoscopy procedure, we first discuss technical aspects of our guidance strategy. Fundamentally, the guidance strategy seamlessly melds the MDCT-based route plan and airway-tree model with the incoming bronchoscope video stream via two major elements:

1. Image registration, to keep the bronchoscope aligned with the MDCT-based route plan.
2. Data fusion, to provide guidance information that facilitates successful navigation and localization.

As alluded earlier, image-guided bronchoscopy systems draw on the premise that an MDCT-based VB view strongly correlates with the structure depicted in the bronchoscopic video frame imaging the same physical view point inside the airway tree. Our system’s image-registration process uses this premise. In particular, it keeps the bronchoscope and MDCT-based route plan aligned by registering the MDCT-based VB views to the live bronchoscopic video. Note that both data sources act as cameras imaging the same 3-D physical space, namely the human chest and airway tree’s endoluminal structure [39], [43].

To this end, let $\mathbf{I}_v^{\Theta_f}$ denote the bronchoscopic video frame i.e., the bronchoscope camera’s view in the video-based “real space”—at pose

$$\Theta_f = (x, y, z, \alpha, \beta, \gamma), \quad (14)$$

where (x, y, z) correspond to 3-D position and (α, β, γ) correspond to the pitch, roll, and yaw angles. Similarly, let $\mathbf{I}_{CT}^{\Theta_v}$ denote a VB view which gives a virtual-camera view at pose Θ_v in the MDCT-based “virtual space.” Image registration involves aligning a given VB view $\mathbf{I}_{CT}^{\Theta_v}$ at known pose Θ_v to a bronchoscopic video frame $\mathbf{I}_v^{\Theta_f}$ at unknown pose Θ_f ; i.e., we seek to find the optimal pose Θ_v^o within a local neighborhood about Θ_v such that

$$\mathbf{I}_{CT}^{\Theta_v^o} \approx \mathbf{I}_v^{\Theta_f}. \quad (15)$$

Stated differently, the optimal pose Θ_v^o that minimizes the difference between $\mathbf{I}_{CT}^{\Theta_v^o}$ and $\mathbf{I}_V^{\Theta_f}$ implies that the two cameras are aligned relative to how they image the same physical space; i.e., each pixel in the two images of (15) observe the same physical location. To solve (15), we use a robust single-frame registration method discussed fully in a companion paper by Merritt *et al.* [39]. The method draws upon the inverse-compositional image-alignment paradigm combined with image-based rendering and can also be used for continuous registration with an incoming video sequence at real-time frame rates.

Data fusion, our guidance strategy's second major element, affects the guidance computer's display during bronchoscopy. To motivate this, first note that the ROIs and associated routes $\{\mathbf{R}_k, \mathbf{r}_k\}$, $k = 1, \dots, K$, airway tree structure $\mathbf{T} = (\mathbf{V}, \mathbf{B}, \mathbf{P})$, and surfaces I_S all reside in the 3-D MDCT-based virtual space. As such, these data sources can be used to create various graphical layers and fused displays to assist with guiding bronchoscopy. In particular, we define two graphical layers:

1. $\mathbf{I}_r^{\Theta}$ derived from the route $\mathbf{r}$ and tree structure $\mathbf{T} = (\mathbf{V}, \mathbf{B}, \mathbf{P})$.
2. $\mathbf{I}_R^{\Theta}$ derived from the corresponding ROI $\mathbf{R}$.

Each graphical layer consists of those parts of the involved structures situated within the range of the virtual camera's 3-D viewing frustum at pose Θ and equals a 2-D image of these structures projected onto the virtual camera's viewing plane. We use these graphical layers to create the following fused views:

$$\text{VB+route fusion: } \mathbf{I}_{CT+r}^{\Theta_v} = \mathbf{I}_{CT}^{\Theta_v} \oplus \mathbf{I}_r^{\Theta_v} \quad (16)$$

$$\text{video+route fusion: } \mathbf{I}_{V+r}^{\Theta_f} = \mathbf{I}_V^{\Theta_f} \oplus \mathbf{I}_r^{\Theta_v^o} \quad (17)$$

$$\text{VB+route/ROI fusion: } \mathbf{I}_{CT+r+R}^{\Theta_v} = \mathbf{I}_{CT}^{\Theta_v} \oplus \mathbf{I}_r^{\Theta_v} \oplus \mathbf{I}_R^{\Theta_v} \quad (18)$$

$$\text{Video+route/ROI fusion: } \mathbf{I}_{V+r+R}^{\Theta_f} = \mathbf{I}_V^{\Theta_f} \oplus \mathbf{I}_r^{\Theta_v^o} \oplus \mathbf{I}_R^{\Theta_v^o} \quad (19)$$

where “ $\oplus$ ” represents an overlay operator; i.e., in (16), a transparent view of $\mathbf{I}_r^{\Theta_v}$ is overlaid pixel by pixel onto the VB view $\mathbf{I}_{CT}^{\Theta_v}$ to create the fused VB view $\mathbf{I}_{CT+r}^{\Theta_v}$. Operations (16) and (18) represent VB views augmented by one or more graphical layers. The video-derived fusion views, (17) and (19), are created after registration of VB view $\mathbf{I}_{CT}^{\Theta_v}$ to a given video frame $\mathbf{I}_V^{\Theta_f}$ per (15). These operations assume that image registration accurately aligns the real and virtual spaces, thereby enabling proper fusion of virtual and real data.

Fortunately, this generally holds true for our method [39]. But, if image registration errors occur, then the mismatch between the two spaces is readily apparent in the fused view.

Fusion views (16) and (17) arise during the navigation phase of bronchoscopy, while views (18) and (19) arise during localization. More specifically, the navigation phase occurs early in bronchoscopy when virtual bronchoscope poses Θ_v situated at view sites $v = v_f$ satisfy the relation

$$\|\mathbf{x}_l - \partial\mathbf{R}\| > \delta \quad (20)$$

for some $\delta > 0$ mm, signifying a lower distance bound from an ROI; i.e., view sites v_f are “far” from ROI $\mathbf{R}$. When bronchoscopy advances far enough along a route—i.e., the virtual bronchoscope’s position no longer satisfies (20) and is approaching $\mathbf{R}$, then the system enters the localization phase. At this point, our system begins to also meld the ROI information $\mathbf{I}_R^\Theta$ into the fused views per (18) and (19).

Algorithm 3

Guidance algorithm along route $\mathbf{r}$ for ROI $\mathbf{R}$. *Italicized lines 7, 14, and 18 indicate steps requiring user input.*

```

1: Inputs:

   bronchoscope video stream  $\mathbf{I}_V^{\Theta_f}$ ,  $f = 1, 2, \dots$ 
   MDCT-based endoluminal surfaces  $I_S$ 
   tree structure  $\mathbf{T} = (\mathbf{V}, \mathbf{B}, \mathbf{P})$ 
   route  $\mathbf{r}$ , ROI  $\mathbf{R}$ 
2: for all branches  $\mathbf{b}_m \in \mathbf{r}$   $m = 1, 2, \dots, a+1$  do
3:   Get next bifurcation point  $v \leftarrow v_{m, \omega_m}$ 
4:   if  $\|v - \mathbf{R}\| > \delta$  then
5:     // Navigation Phase:
6:     Present VB view  $\mathbf{I}_{CT+r}^{\Theta_v}$  per (16) at next bifurcation
7:     Physician moves bronchoscope close to  $\mathbf{I}_{CT+r}^{\Theta_v}$ 
8:     Capture video frame  $\mathbf{I}_V^{\Theta_f}$ 
9:     Register MDCT virtual space to bronchoscope’s real space
         $\rightarrow \Theta_v^o$  found such that  $\mathbf{I}_{CT}^{\Theta_v^o} \approx \mathbf{I}_V^{\Theta_f}$ 
10:    Present fused video/route view  $\mathbf{I}_{V+r}^{\Theta_f}$  per (17)
11:   else
12:     // Localization Phase:

```

```

13: Present VB view  $\mathbf{I}_{CT+r+R}^{\Theta_v}$  per (18) at next bifurcation
14: Physician moves bronchoscope close to  $\mathbf{I}_{CT+r+R}^{\Theta_v}$ 
15: Capture video frame  $\mathbf{I}_V^{\Theta_f}$ 
16: Register MDCT virtual space to bronchoscope's real space
     $\rightarrow \Theta_v^o$  found such that  $\mathbf{I}_{CT}^{\Theta_v^o} \approx \mathbf{I}_V^{\Theta_f}$ 
17: Present fused video/route/ROI view  $\mathbf{I}_{V+r+R}^{\Theta_f}$  per (19)
18: while Physician moves bronchoscope do
19:     Capture video frame  $\mathbf{I}_V^{\Theta_f}$  and register spaces
20:     Present updated fused view  $\mathbf{I}_{V+r+R}^{\Theta_f}$ 
21: end while
22: end if
23: end for

```

Given this discussion, Algorithm 3 details the guidance strategy. The system inputs are the ROI $\mathbf{R}$, route $\mathbf{r}$ as in (9–11), the full original tree structure $\mathbf{T}$, and the airway surfaces I_S . The goal is to offer guidance cues at key decision points along a route, namely the bifurcation points, to help the physician advance properly. As such, the method focuses on discrete registration events at each bifurcation point to keep the virtual and real spaces aligned. The system begins guidance by presenting the VB/route view $\mathbf{I}_{CT+r}^{\Theta_{1,\omega_1}}$ situated at the end of first branch $\mathbf{b}_1$; i.e., at the main carina $\mathbf{v} = \mathbf{v}_{1,\omega_1}$ (line 6). The physician then moves the bronchoscope close to this position and holds steady. The system then captures a video frame $\mathbf{I}_V^{\Theta_1}$, performs registration, and presents the first fused video/route view $\mathbf{I}_{V+r}^{\Theta_1}$ (lines 8–10).

This process continues for subsequent route bifurcations. Depending on whether bronchoscopy is in the navigation (lines 4–10) or localization phase (lines 11–22), the system computes and displays the appropriate video-derived fusion view, $\mathbf{I}_{V+r}^{\Theta_f}$ or $\mathbf{I}_{V+r+R}^{\Theta_f}$, with each view showing the current location in relation to the MDCT-derived route-planning structures. During the final approach to the ROI (lines 18–21), the algorithm performs continuous video registration until the end of the procedure. Fig. 6 illustrates the registration/fusion process along a route segment and depicts example fusion views.

For clarity, Algorithm 3 assumes that the terminating view site for branch $\mathbf{b}_{a+1}$ is, of course, the destination $\mathbf{v}_D$, following (11). We comment below on a few variants in our real computer implementation. First, after the initial registration at line 9, the physician can optionally invoke continuous registration/tracking on the incoming video. This option enables a continuous update of the various displays, while the physician freely moves the

bronchoscope. As Section III points out, however, this approach tends to be impractical for peripheral nodules. This is because bronchoscope maneuvers become much more challenging and require more halting, hovering, or repeat attempts in the peripheral airways.

Another variant allows the physician to halt navigation (at line 9), back up to a previously saved “base camp” location, and then resume navigation. This invaluable feature, discussed more below, helps the physician reconsider and recover from difficult bronchoscope maneuvers. It also serves as a fail safe if registration goes off track; e.g., the physician is getting lost because of a coughing episode.

Note that previous works have suggested using a transparency-based rendering to fuse route and ROI information with the VB views and bronchoscopic video [6], [43]. Using the ideas of [6], [43], the ROI increases in size in the fused views as the physician navigates closer toward an ROI—this gives the visual cue that the bronchoscope is approaching the ROI. Unfortunately, this mechanism still results in an ambiguity in the ROI’s actual location, because size does not indicate proximity. This issue is especially problematic during localization. One of our solutions to this issue is to delay introduction of ROI information into the fused views until entering a defined localization phase via (18–20). In addition, our implementation of the graphical layer $\mathbf{I}_r$ adds a new graphical icon—a fixed-size arrow—that appears at route destination $\mathbf{v}_D$ in the fused views; e.g., Figs. 6(d) and 7(f). As later examples show, these ideas greatly help to confirm that a desired biopsy site is within the current bronchoscope FOV.

We now describe system interaction during live bronchoscopy. Following Fig. 2(b), a technician initializes the guidance computer by interfacing it to the bronchoscope’s video processor; this starts a live video feed. The guidance computer’s display is also preset to the beginning of the first target $\mathbf{R}_1$ ’s preplanned airway route $\mathbf{r}_1$. During bronchoscopy, the display continuously presents and updates two viewers.

1. A 3-D airway-tree viewer, which gives a global surface rendering of the airway tree, guidance route, target site, and current virtual-bronchoscope position.
2. An Endoluminal Viewer, which contains two separate panels. A live panel simultaneously shows the live bronchoscopic video and the next target VB view along the airway route. A base camp panel shows a frozen view of a registered video frame and VB view of a previously visited airway location along the route (the “base camp”).

In all display components, the route unambiguously indicates the correct route $\mathbf{r}_1$ to follow in blue, while incorrect airway options—i.e., branches $\mathbf{b}_m \notin \mathbf{r}_1$ —appear in red. In addition, to help the physician ascertain progress toward the target, the display also continuously provides the bronchoscope’s current distance from the target. Fig. 5(b), discussed later, gives an example display.

To begin the navigation phase per Algorithm 3, the physician advances the bronchoscope to a location close to the Endoluminal Viewer’s initial VB view. The VB view is then registered to the bronchoscopic video. This synchronizes the “virtual” 3-D MDCT space to the “real” bronchoscope space, enabling subsequent fusion of MDCT information and

bronchoscopic video. The system updates the base camp view to save the synchronized display, advances the Endoluminal Viewer's live panel to the next airway bifurcation along the route, and the process is repeated. As mentioned earlier, the base camp saves a fall-back point in case the physician becomes uncertain of the bronchoscope's current location (e.g., during patient coughing)—he/she can back up to the unambiguously correct base camp and restart navigation.

When the physician maneuvers to within δ mm of $\mathbf{R}_1$, the localization phase begins. We default $\delta = 40$ mm in (20). The system now provides additional visual cues in the Endoluminal Viewer to assist with final target localization: 1) a transparent target view and 2) a 4-mm-long arrow emanating from the destination and aimed at the target surface $\mathbf{R}_1$. (Figs. 6 and 7 give examples.) Throughout guidance, fusion of MDCT-based information onto the bronchoscopic video occurs. In addition, the system continuously updates two forms of global distance information: 1) distance from the bronchoscope tip to the ROI centroid; 2) minimum distance from the bronchoscope tip to any visible point of $\mathbf{R}_1$. Also, during localization, the physician can hover the guidance computer's mouse over a pixel in the fused views $\mathbf{I}_{CT+r+R}^{\Theta_v}$ or $\mathbf{I}_{V+r+R}^{\Theta_f}$ to garner other distance information: 1) distance from the bronchoscope tip to the airway wall's surface and 2) distance from the bronchoscope tip to the ROI's surface. The physician uses these data to perform a final maneuver toward the target and obtain the requisite tissue sample. The process is then repeated for the next target $\mathbf{R}_2$.

D. Implementation Details

Considering human-factor engineering, we mandated that the system should integrate smoothly into the clinical work flow without unduly distracting the busy physician. As such, for a typical study, 3-D MDCT analysis took on the order of 10 min for all operations, including the interaction required to define ROIs (see Section III-B). For image-guided bronchoscopy, we required that the system provide prompt feedback so that intraprocedure errors could be immediately recognized, thus ending the “guess and check” approach that has long characterized bronchoscopy. Also, we integrated all guidance information and bronchoscopy video onto a single monitor rather than at spatially disparate locations.

All processing can easily be performed on a mid-range PC. During our prototyping studies, however, we employed a separate PC for the offline 3-D MDCT analysis. For image-guided bronchoscopy, we used a second computer mounted on a compact mobile cart, equipped with a 24-in monitor. Also, as stated earlier, we used a tablet PC for route inspection (Lenovo X60). For our most recent studies, we employed a Dell Precision T7500 PC (2.8 GHz Xeon X5660 dual CPU, NVidia Quadro 4000 video card, 512 MB video memory) equipped with a Matrox Solios frame grabber for real-time video capture. We developed all software using Visual C++ with certain graphics functions based on OpenGL [46].

A patient study generally involves <5 target ROIs. Regarding ROI shapes, suspect nodules and lymph nodes generally have a long-axis length > 10 mm, while lavage, brush, and airway-exam sites by definition terminate inside an airway and have no relevant “diameter” [5]. We point out that the computed route directions are specific for a given route. Our

method for calculating VB views and airway-tree renderings is well known, drawing upon the MDCT scan I , airway-tree surfaces I_S , and the Marching Cubes algorithm [43], [47]. All rendering calculations, including the data-fusion operations, were implemented using OpenGL and custom code [6], [46].

Note that each ROI for a given patient may demand different route constraints. For example, a lymph node $\mathbf{R}_1$ may require a needle biopsy, while a cancer-infiltrate site $\mathbf{R}_2$ may call for a BAL. For this situation, route planning can be run two separate times, using different values for the procedural constraint n_L in (6); e.g., $n_L = 30$ mm for the needle biopsy, and $n_L = 0$ mm for the BAL. In addition, it is common to use multiple bronchoscopes to examine a patient. Again, it is straightforward to invoke route planning multiple times to accommodate each device. Later, during bronchoscopy, switching bronchoscopes results in no unusual procedural delay, as our system automatically adjusts for the new bronchoscope's optical FOV through an ROI's stored route specifications.

A major reason our system succeeds during bronchoscopy is the speed of our registration method. As discussed in the companion paper by Merritt *et al.*, the method can perform registrations at a rate of 300 frames/s, a rate far above the bronchoscope's video frame rate of 30 frames/s [39]. This efficiency enables our system to perform continuous real-time data fusion and display updates during bronchoscopy. Finally, note that all quantitative information constituting the procedure plan, including the airway tree model, routes, and ROIs, is known and stored. Therefore, the continuously updated distance measures presented during live bronchoscopy require only a simple data look up.

III. Results

Section III-A first illustrates the performance of the route-planning methods in an image-only study, supplemented by a profile of typical airway-tree characteristics as observed in a database of MDCT chest scans. Section III-B then presents a peripheral-bronchoscopy patient study that exercises our complete system within the demanding work flow of a real-time clinical setting. We also benchmark our system's results for ultrathin bronchoscopy against those obtained in clinical studies derived with an existing image-based guidance system.

A. Retrospective Image-Only Studies

We tested the route-planning methods of Algorithms 1 and 2 in a 10-patient MDCT-only retrospective study. The goal was to study method performance up to 3-D MDCT analysis. The MDCT scans for cases 1 and 2 and 6–9 were collected with a PhilipsMx8000 four-detector scanner, while the scans for cases 3–5 and 10 were collected with a Siemens Sensation-16 16-detector scanner. The number of 2-D sections ranged from 193 to 706. Axial-plane resolution (x , y) ranged between 0.55 and 0.81 mm. For the Philips cases, section spacing $z = 0.5$ or 0.6 mm, with section thickness = 1 mm. For Siemens cases 3–5, $z = 1.0$ mm and section thickness = 1.5 mm. Fig. 1 gives the details for Siemens case 10. A physician used the 3-D live wire to define 11 total ROIs for the 10 cases, with two ROIs defined for case 1. The ROIs consisted of suspect peripheral nodules and infiltrates

distributed over all five lobes of the two lungs. Eight of eleven ROIs were situated outside the airways.

For constraint (6), we required feasible routes to terminate $<n_L = 40$ mm from an ROI's surface. We also required feasible routes to accommodate an Olympus ultrathin BF XP160F bronchoscope (see Table I). Note that the XP160F is a standard commercial device for peripheral bronchoscopy. As listed in Table I, the XP160F introduces constraint $d_B = 2.8$ mm. Because this device has a large bending range and a nominal FOV value $\theta_{FOV} = 120^\circ$, we can effectively set $\theta_B = 180^\circ$. In addition, we employed two FOV values in the study: $\theta_{FOV} = 180^\circ$ or 70° .

The choice $\theta_{FOV} = 180^\circ$ essentially implies that any bronchoscope maneuver is feasible. While this is within the realm of reason for the ultrathin bronchoscope, it does not account for several factors. First, a bronchoscope can be difficult to maneuver in the periphery, as the airways get shorter and bifurcate more frequently; see Section III-B. In addition, we recommend building in a guard band into the FOV to account for patient breathing and potential airway collapse and to emphasize the need for a clear ROI view at the destination $\mathbf{v}_D$ within bronchoscope's FOV center. Finally, the distortion correction that we apply to the video, a necessary operation for registration, expands the video FOV slightly [48]. For these reasons, we have favored the more restrictive $\theta_{FOV} = 70^\circ$. Note that bronchoscopes can have more restrictive FOVs than the devices listed in Table I. For example, the Olympus BF-UC160F-0L8 bronchoscope has tip-bending angles 120° up and 90° down, $\theta_{FOV} = 80^\circ$, and $d_B = 6.9$ mm. Hence, angular restrictions are vital to consider.

After running optimal route planning for the various cases, we performed report inspection. Note that in our implementation of Algorithm 1, we actually save the top $N = 5$ closest routes, regardless of whether they meet restriction (6). In this way, we could examine multiple options during report inspection to establish ground truth and correctness.

Table II summarizes the results. The default constraints for case 1's ROI 1 produced a feasible 9-generation route. To understand the impact of the constraints, we performed two additional trials for this ROI. For trial 2, we unconstrained the scope diameter. As expected, resulting in a route terminating closer to the ROI; interestingly, the route used fewer airways and approached the ROI from a different final—and narrower—airway. Note that peripheral nodules situated inside the lungs typically reside near a “bundle” of airways; i.e., within a subsegment of a lung lobe. Hence, different routes can approach an ROI locally from different directions. By varying route constraints, we can study such variations offline prior to bronchoscopy. Finally, using the stringent $\theta_{FOV} = 70^\circ$ for trial 3 of case 1's ROI 1, the optimal route resided nearly 70 mm from the destination. For case 2, the more stringent θ_{FOV} also did not produce an acceptably close route. For case 3, we ran one trial with the default constraints and a second with a combination of a relaxed d_B and tighter θ_{FOV} . These trials produced routes which differed at the terminal airways. For case 4, the default parameters did not result in a suitably close route, even though the minimum airway diameter encountered (3.3 mm) could easily accommodate the bronchoscope; evidently, any added branch involved a constricted airway which inhibited finding a suitably close route. Relaxing d_B produced an acceptably close route, but revealed a 1.5-mm constriction. For

cases 6–10, we exclusively employed the tighter FOV constraint—all cases produced sufficiently close optimal routes. Finally, notice that the optimal routes for the cases having endoluminal ROIs (cases 6, 7, 10) resulted in routes terminating < 5 mm from the ROI.

To help understand human airway-tree geometry, as it pertains to bronchoscopy route planning, we next present a study of the morphological characteristics of the human airway tree within the context of a large human database [49]. This study also helps to place the peripheral-bronchoscopy study of Section III-B in a practical context. To this end, we assembled a database of 81 MDCT scans obtained from lung-cancer patients collected under informed consent for two IRB protocols. These scans were drawn from several other studies: 1) a mediastinal bronchoscopy study discussed in the companion paper by Merritt *et al.* [39]; 2) a central-chest lymph-node study presented by Lu *et al.* [50]; 3) the peripheral-bronchoscopy study presented in the next section; and 4) other data collected for ongoing studies.

The scans were produced by either a Siemens Sensation-16, Emotion-40, or Definition-64 MDCT scanner. 3-D images were reconstructed to give contiguous 0.75-mm-thick axialplane sections spaced $\Delta z = 0.5$ mm apart. Axial-plane resolution ($\Delta x, \Delta y$) ranged between 0.40 and 0.92 mm and the number of sections ranged between 99 and 830. One scan was from a PET-CT scanner. For all scans, we ran airway-tree model calculation, per Fig. 2(a). We then compiled the mean characteristics of the airway trees. The results, tabulated in Table III, give a profile of the average diameter and length of constituent airway branches, along with a measure of branch angle between parent and child branches. The table also lists how many cases out of 81 have at least one branch at a particular generation and the total number of branches found over the database at a given generation index. We point out that these cases are representative of the patient population that comes through our University Hospital's pulmonary medicine practice. Hence, we believe Table III is also representative of the U.S. population overall.

Nearly 100% of the scans (78/81) could accommodate the ultrathin bronchoscope for at least one generation-10 airway; i.e., they have airways with $d_I > 2.8$ mm in diameter. Furthermore, over half of the scans (49/81) contained sufficiently large airways for ultrathin bronchoscopy at generation 13 or greater. Regarding branch length, the left main bronchus is, of course, substantially longer than the right main bronchus. While airway length varies substantially at lower generations, the mean branch length tends to be on the order of 10 mm, even for airways at generation 10. Interestingly, the mean branch angle θ_I consistently tends to be on the order of 40° . These observations imply that peripheral navigation of an ultrathin bronchoscope is clearly feasible deep into the airway tree. We caution, however, that sharp turns on the order of $\theta_I = 70^\circ$ do arise in many occasions.

Table III gives results over raw generation index, without regard to the configuration and connectivity of the five lung lobes. In particular, the right intermediate bronchus serves as a parent to the right middle-lobe bronchus and right lower lobe bronchus, the major airways entering the right middle and right lower lobes. Also, the major airway leading into the left upper lobe also serves as a parent to the left lingular region. If one takes into account these relationships and instead considers lobar parent airways to be at the same generation index,

then Table III changes slightly, but essentially all observations above remain approximately the same. See [49] for more.

B. Live Human Studies

We next evaluated our complete system's performance for peripheral bronchoscopy in a prospective clinical human study. Under a Penn State IRB protocol, we enrolled and consented 30 patients, encountered in our University Hospital's lung-cancer management clinic, who were scheduled for diagnostic bronchoscopy and exhibited peripheral lesions on their MDCT scans. The 30 patients included 21 women and 9 men (ages, 18–85 years; mean, 60.6 ± 16 [mean $\pm$ standard deviation]). The MDCT scans were produced using either a Siemens Sensation-16, Emotion-40, or Definition-64 MDCT scanner and reconstructed to give contiguous 0.75-mm-thick axial-plane sections spaced $z = 0.5$ mm apart. Axial-plane resolution (x , y) ranged between 0.52 and 0.92 mm.

The physician defined a total of 69 target ROI sites for the 30 cases (median, two targets/case; range, 1–5) (see Table IV). All ROIs were situated at a depth ≤ 4 airways (trachea = generation 1) and had a mean diameter = 21 mm (range, 4–66 mm). The physician chose bronchoscopes from the three devices listed in Table I. The physician used the ultrathin bronchoscope for peripheral navigation, collecting diagnostic samples with either a cytology brush (Olympus BC-203D-1006), 50 ml BAL, or biopsy forceps (Olympus FB-56D-1). When possible, one of the large bronchoscopes, which have a bigger working channel, was used to allow for aspiration needles. The physician employed the ultrathin bronchoscope exclusively for 45 targets, two bronchoscopes (ultrathin and large) for 8 targets, and a large bronchoscope exclusively for 16 targets. For the purpose of optimal route planning, we used $n_L = 30$ mm.

During bronchoscopy, patients underwent topical lidocaine airway anesthesia (300 ± 100 mg) and sedation using standard clinical protocol (conscious sedation, $n = 12$; deep sedation, $n = 14$; hybrid, $n = 4$). Median midazolam dose was 6 mg (range, 0–9 mg), median fentanyl dose was 125 mcg (range, 0–175 mcg), and median propofol dose was 290 mg (range 80–600 mg). Radiographic fluoroscopy was available when requested. Tissue samples were sent to the pathology laboratory for analysis. For every patient, we recorded the computer display and bronchoscopic video for an entire procedure.

Two technicians retrospectively and independently analyzed the recorded computer display and bronchoscopic video for each patient. A technician determined the bronchoscope's location by comparing the recorded bronchoscopic video to the reconstructed VB airway-tree model in tandem with the patient's MDCT scan. Also, we verified all computed routes and associated VB images to be correct, as determined by visual inspection of the prebronchoscopy reports and MDCT. We considered five metrics to measure the predictive behavior of our route-planning methods and the efficacy of our guidance system.

1. Predicted bronchoscope insertion depth, defined as the number of airways constituting the MDCT-based optimal endobronchial guidance route leading to an ROI.

2. Actual bronchoscope insertion depth, defined as the actual number of airways traversed by the physician during image-guided bronchoscopy.
3. Navigation success, defined as correctly guiding the bronchoscope to the final preplanned target airway.
4. Time until first sample, defined as the time required for guiding the physician to a target ROI.
5. Tissue-sampling success, defined as the collection of a satisfactory tissue sample.

These metrics have also been used in other bronchoscopy studies [8], [22], [23]. Measure (1), computed during optimal route planning, represents the expected number of airways that the physician would be able to insert a selected bronchoscope during image-guided bronchoscopy. A tissue sample was deemed satisfactory if it was so stated by the pathologist on the clinical synoptic report.

Tables V–VI summarize numerical results for all target ROIs, while Table VII summarizes results for successful navigation. Fig. 7 depicts image-guided bronchoscopy progress along a route for a nodule impinging on a generation-13 airway.

Per Tables V–VI, the system on average gave a predicted bronchoscope insertion depth of 7.3 ± 2.3 airways toward a target (median, 7; range, 4–12), with the mean diameter of a route's terminal airway = 3.9 ± 1.5 mm (median, 3.2 mm; range, 2.4–9.0 mm). (Note that the lymph nodes, being located in the chest's mediastinal region, are located at a shallower depth in general than peripheral targets.) During bronchoscopy, the bronchoscopist achieved a mean actual bronchoscope insertion depth of 7.1 ± 2.4 airways (median, 7; range, 3–13), with the mean diameter of the final traversed airway = 4.3 ± 2.1 mm (median, 3.7 mm; range, 2.3–11.0 mm). For the target subset examined via ultrathin bronchoscopy (45/69), our system produced endobronchial routes having a mean predicted bronchoscope insertion depth of 8.2 ± 2.1 airways, while during image-guided bronchoscopy, the system facilitated a mean actual bronchoscope insertion depth of 8.0 ± 2.0 airways. Notably, 10 routes traversed 10 airways.

Thirty target sites were situated outside an airway. For these extraluminal targets, the MDCT-based endobronchial route terminated at the airway-wall location closest to the target's surface; the mean distance from the airway wall to the target's surface was 3.6 ± 3.7 mm (median, 2.0 mm; range, 0–14.4 mm).

As shown in Table VII, successful navigation occurred for 63/69 (91%) targets. Breaking these results down by lobar region (cf. Tables IV and VII), successful navigation occurred for 17/18 (94%) RUL targets, 11/12 (92%) RML targets, 11/12 (92%) RLL targets, 21/22 (95%) LUL targets, and 3/5 (60%) LLL targets. For the 63 correctly navigated targets, the actual bronchoscope insertion depth of 7.3 ± 2.4 airways was virtually identical to the system's predicted bronchoscope insertion depth of 7.3 ± 2.3 airways.

Retrospective analyses of the procedure videos revealed that two navigation failures occurred because the video feed and VB view were not correctly synchronized, while the remaining four navigation failures were preventable, as the physician clearly knew the

correct branch to enter but did not maneuver the bronchoscope correctly. Notably, these failures occurred at airway branch points that required the physician to perform a difficult maneuver. Given that our system always enables direct vision, the physician could see the correct airway to maneuver into, but could not move forward without first backtracking and moving forward with momentum. Along this line, patient cough and dynamic airway collapse forced the physician to retreat several airway generations. The physician then attempted to return to the site from memory, but sampled from an incorrect location.

From Table IV, 62 targets required a tissue sample, while the remaining seven targets only involved visual inspection. For the 62 targets requiring a tissue sample, successful navigation occurred for 57/62 (92%) targets. We collected satisfactory samples for 52/62 (84%) of these targets, where the five navigation failures were designated as sites not giving satisfactory samples. These samples enabled a diagnostic yield of 69% for the 29 of 30 patients in which diagnostic tissue was successfully obtained.

As referenced earlier, several clinical studies have shown the considerable promise of VB-only techniques for planning and guiding bronchoscopy to the lung periphery. In particular, Shinagawa, Asano and colleagues performed several clinical studies that represent the current standard for peripheral bronchoscopy practice [8], [22]–[24]. In their studies, they employed a prototype of a commercial VB-based guidance system that, like other purely image-based guidance systems, requires no elaborate sensor hardware; they also employed the same model ultrathin bronchoscope used in our study.

Along this line, we benchmarked our system versus the ultrathin bronchoscopy study of Shinagawa *et al.* [22], [23]—see Table VII. For ultrathin bronchoscopy, our system facilitated a mean actual bronchoscope insertion depth = 8.3 ± 1.9 airways, while Shinagawa *et al.* reported a mean actual bronchoscope insertion depth = 5.7 ± 1.3 airways. Our results represent a statistically significant increase of over two airways for bronchoscope navigation over the system tested by Shinagawa *et al.* ($p < 0.0001$). (As is commonly done in making statistical comparisons between two independent studies, we assumed that their respective results abide by normal distributions and, thus, use the Student's t-test to compute significance measures.) Our results also greatly exceed those in another study by Asano *et al.* using the same system, with a reported median bronchoscope insertion depth = 6 [8]. In fact, for all ROIs we considered, including those examined with the two large-diameter bronchoscopes, we still navigated substantially deeper on average (mean actual bronchoscope insertion depth = 7.3 ± 2.4 airways) than the related studies. In addition, the other studies reported no navigated routes spanning 10 airways. This implies a significant restriction on the ability to perform bronchoscopy deep into the periphery. Observe that Table III indicates that most patients exhibit many airways at generation 10 in their MDCT scans. Also, nearly one-sixth of our targets involved routes at this depth.

The mean time to first sample using our system was $5:15 \pm 5:06$ min (median, 3:40 min; range, 0:25–32:07 min). For ultrathin bronchoscopy, our mean time to first sample of $6:48 \pm 5:40$ min (median, 5:38 min; range, 0:50–32:07 min) was significantly shorter than the time of $8:30 \pm 4:42$ min reported by Shinagawa *et al.* ($p=0.0834$) [22]. In addition, Shinagawa *et al.* reported a 66% diagnostic yield versus our rate of 69% (they did not report

on navigation success). We believe that our system's substantially shorter guidance time is especially striking, given that our target ROIs were situated over two airways deeper on average than the target ROIs considered by Shinagawa *et al.*

While the other studies do not quote MDCT analysis time, they do outline a cumbersome interactive method that requires either a radiologist or experienced technician to manually define airway routes and associated VB views along a route from the MDCT scan, a process that likely accounts for their restricted route depths. Our system, on the other hand, required little interaction time on average. In particular, over five consecutive cases, ROI definition required 2:30 to define each ROI, with a technician performing all live-wire analysis when needed. Subsequent 3-D airway-tree model calculation and optimal route planning then ran *automatically* in 6:30 per case, based on nonoptimized computer code.

IV. Discussion

With the widespread usage of MDCT scanners coupled with ultrathin bronchoscopes, the application of bronchoscopy for diagnosing peripheral nodules is becoming a viable option [1], [2], [4], [51]. MDCT scanners enable the detection of airways approaching 1 mm in diameter, while ultrathin bronchoscopes allow navigation through over ten airway generations under direct vision. Also, bronchoscopy to the lung periphery has potential for thoracic-surgery planning and for the deployment of focal treatment and drug delivery, especially in light of the burgeoning activity toward cancer biomarker identification [52]. Yet, route planning based on mental reading of an MDCT scan results in errors as early as a second-generation airway, while bronchoscope navigation for peripheral-nodule biopsy based on standard axial-CT exam results in diagnostic rates ranging from 14%–77% [7]–[9], [13].

A fundamental upgrade to the bronchoscopy planning and guidance process could mitigate these issues, especially given the recent advances in imaging science for image-guided intervention systems. Our system accomplishes this upgrade by incorporating an extensive set of features motivated by image-processing and computer-graphics techniques. Automated image-processing techniques and complementary computer-graphics methods better exploit the extensive information inherent in a 3-D MDCT chest scan. Image processing enables rapid optimal route planning and report generation. Computer graphics enables augmented airway/lung visualizations beyond simple 2-D axial-plane images and admits the possibility of data fusion between the MDCT scan and live bronchoscopic procedural video.

We strongly caution, however, that we can only make a historical comparison between our system and previous systems, as we did not compare our system to others directly in a randomized control trial. Also, our results can be attributed to patient selection bias. Nevertheless, our results do represent a new and substantially higher upper bound on bronchoscope navigation depth than previously reported. We also point out that the system employed by the earlier studies had the significant ergonomic disadvantage of using two monitors: one monitor for presenting the standard bronchoscopic video and a second monitor for displaying the MDCT-based guidance information.

As mentioned earlier, some ROIs pose special navigation challenges, independent of a guidance system's effectiveness. This is in line with the known difficulties in maneuvering an ultrathin bronchoscope deep into the lung periphery, where the airways become shorter and bifurcations occur more quickly (see Table III) [8], [14], [23]. Also, breathing-cycle-dependent airway collapses and secretions can hinder navigation. In our studies, the physician often had to make several repeat attempts at complex "gymnastics maneuvers" through two or three successive short airways without stopping.

For example, Fig. 8 depicts a problematic location for the ROI requiring the longest navigation time (32:07) in our study, with Fig. 5(b) depicting a system view just before navigation became difficult. While this ROI was located only eight generations deep into the airways, most of the guidance time involved a single maneuver, which required the physician to insert the bronchoscope into a small orifice at an unusually sharp branching angle. The orifice, shown in Fig. 8(c), led to an aberrant segment incident upon the lingular bronchus and occurred only four generations along the route. Yet, while physician clearly knew the route, completing the maneuver required many attempts. Notably, the procedure was delayed by the patient's airways exhibiting significant bleeding and requiring repeated cleaning.

We note in passing that deep peripheral sites can involve slight route adjustments prior to bronchoscopy, which can be noted during report inspection [38], [53]. In addition, there are known challenges in peripheral bronchoscopy in terms of effective tissue sampling, which arise beyond the efficacy of a guidance system. Yet, given that effective guidance to the lung periphery is now possible, the continued development of suitable instruments could ameliorate these difficulties.

The proposed route planning methods can conceivably be augmented with other constraints. For instance, the notion of obstacles could be incorporated. More specifically, if the physician punctures a vessel, then this could result in a life-threatening event. Similarly, the puncture of the lung boundary could lead to pneumothorax. Hence, blood vessels and the lung boundaries can be introduced as obstacles to avoid in route planning, i.e., a constraint can be introduced whereby a needle extending from the bronchoscope tip cannot pass through or near an obstacle. Conversely, if a suspect nodule exists within a specific lung lobe, then an anatomical requirement can be imposed whereby a feasible route must terminate within the required lobe. Another possibility is to use a needle placement strategy to optimize the amount of tissue sampled [54]. Similarly, the bronchoscope's diagnostic FOV constraint can be augmented by requiring a route's destination $\mathbf{v}_D$ to subtend a sufficient fraction of an ROI's total volume, thereby better ensuring a large tissue biopsy. Finally, the viewing directions can be further modified. In particular, standard bronchoscopy practice often dictates canonical bronchoscope positions for the major airways entering the lung lobes.

V. Conclusion

We presented an image-based planning and guidance system that significantly improves upon other proposed systems for peripheral bronchoscopy. It offers the following advances:

1) optimal route planning, which gives accurate airway routes to arbitrarily selected target sites; 2) an interactive prebronchoscopy report that enables the physician to preview a procedure in advance; 3) a guidance display that integrates all views on one monitor during bronchoscopy, including the bronchoscopic video, affording better perception; 4) data fusion between the MDCT-based planning data and bronchoscopic video to give augmented visual and quantitative information during both bronchoscope navigation and ROI localization; and 5) registration of the VB-based guidance route with the bronchoscopic video, in addition to a fall-back “base camp” view, to facilitate data fusion and complex bronchoscope navigation and error recovery. Features (1–2) introduce a holistic route-planning approach that gives guidance information before and during a procedure, while features (3–5) upgrade procedure guidance by greatly augmenting the physician’s vision and comprehension. Our system requires minimal interaction, with the physician’s interactions limited to ROI selection and prebronchoscopy report perusal. A technician quickly performed any required ROI definition, with most other operations being automatic. In live human studies, the system functioned smoothly with no adverse events for all patients.

For ultrathin bronchoscopy, our system’s optimal route planning method predicted a mean bronchoscope insertion depth of 8.2 airways per target, while the mean actual bronchoscope insertion depth during live guided bronchoscopy was 8.3 airways. Also, our mean time to first biopsy sample was 6:48 (min:s). As a comparison, a related ultrathin bronchoscopy study performed with a competing commercial system achieved a mean bronchoscope insertion depth of 5.7 airways and a mean time to first sample of 8:30. Thus, our system enabled bronchoscopy over two airways deeper into the airway-tree periphery, with a sample time that was nearly 2 min shorter on average. In addition, our system’s ability to almost perfectly predict the depth of a bronchoscope’s navigable route in advance represents a substantial benefit of optimal route planning.

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Biographies

Jason D. Gibbs received the B.S. and M.S. degrees in electrical engineering from Binghamton University, Binghamton, NY, USA, and the Ph.D. degree in electrical engineering from The Pennsylvania State University, University Park, PA, USA.

He is currently working at Broncus Medical, Inc., Mountain View, CA, USA, and State College, PA, where he is involved in research and development in the general areas of medical image analysis and image-guided intervention systems.

Michael W. Graham received the B.S., M.S., and Ph.D. degrees in electrical engineering from The Pennsylvania State University, University Park, PA, USA.

He has worked for the Teach for America program of Americorps previously. He is currently working as a Software Engineer at Google, Inc., Pittsburgh, PA. His research interests

include 3-D medical image processing and visualization, algorithm design and analysis, machine learning, and pattern recognition.

Rebecca Bascom received the A.B. degree in french studies from Harvard University, Cambridge, MA, USA, the M.D. degree from the Oregon Health Sciences University, Portland, OR, USA, and the M.PH. degree from Johns Hopkins University, Baltimore, MD, USA.

She was with the University of Maryland and Johns Hopkins University previously. She is currently a Professor of medicine at the Penn State Milton S. Hershey Medical Center, Hershey, PA, USA. Her research interests include the areas of pulmonary medicine, lung toxicology, and occupational health.

Duane C. Cornish received the B.S. and Ph.D. degrees in computer science from The Pennsylvania State University, University Park, PA, USA.

He is currently working as a Senior Software Developer at Johns Hopkins University, Applied Physics Lab, Laurel, MD, USA. His research interests include 3-D medical image processing and visualization.

Rahul Khare received the B.E. in electronics engineering from Mumbai University, Mumbai, India, and the M.S., and Ph.D. degrees in electrical engineering from the Pennsylvania State University, University Park, PA, USA.

He previously held a position at Video Mining, Inc., State College, PA, USA. He is currently a Postdoctoral Fellow in the Sheikh Zayed Institute, Children's National Medical Center, Washington, DC, USA. His research interests include 3-D medical image processing and visualization, computer vision, machine learning, and pattern recognition.

William E. Higgins (F'03) received the B.S. degree in electrical engineering from the Massachusetts Institute of Technology, Cambridge, MA, USA, and the M.S. and Ph.D. degrees in electrical engineering from the University of Illinois, Urbana-Champaign, IL, USA.

He has held positions previously at the Honeywell Systems and Research Center, Minneapolis, MN, USA, and the Mayo Clinic, Rochester, MN, USA. He is currently a Distinguished Professor of electrical engineering, computer science and engineering, and bioengineering at the Pennsylvania State University, University Park, PA, USA. His research interests include multidimensional medical image processing, virtual endoscopy, and image-guided intervention systems, with an emphasis on applications for the chest.

Fig. 1.

Illustration of the hazards in using interactive route selection automated 3-D airway-tree segmentation and centerline-line definition was first applied to the 3-D MDCT scan [28], [29]. (a) Weighted-sum coronal-plane projection of the MDCT scan and extracted red centerlines, along with a preselected green ROI. The user interactively chose the route shown in yellow. This view appears to indicate that the route properly approaches the ROI. (b) Sagittal-plane projection shows that the selected route terminates in the anterior of the chest, while the ROI lies in the posterior. (Case 21405-3a; MDCT image specifications: $x = y = 0.67$ mm, section spacing $z = 0.5$ mm, 706 0.75-mm thick sections.) (a) Coronal projection. (b) Sagittal projection.

Fig. 2.

Two-stage work flow for the proposed image-guided bronchoscopy system. (a) Stage 1: 3-D MDCT analysis. (b) Stage 2: Image-guided bronchoscopy.

Fig. 3.

Example of 3-D MDCT analysis. (a) Physician indicates a target ROI on a 2-D axial-plane section of the patient's 3-D MDCT chest scan; the figure shows an application of the 2-D live wire to a 13-mm-diameter left upper-lobe solitary pulmonary nodule on section $z = 331$ [41]. (b) Automatic methods extract a patient-specific 3-D airway-tree model, consisting of the endoluminal and extraluminal surfaces of the 3-D airway tree (tan structure) and airway centerlines (red lines), with the previously defined target nodule shown in green [6], [30], [43]. (c) Automatic route planning defines the optimal 3-D endobronchial route (blue line) leading to the target. The illustrated route ends at a generation-8 branch. (Case 20349-3-25; MDCT image specifications: $x = y = 0.86$ mm, $z = 0.5$ mm, 796 0.75-mm thick sections.). (a) ROI definition. (b) 3-D Airway-Tree Model. (c) Route planning.

Fig. 4. Illustration of route-planning constraints. (a) Bronchoscope tip model, depicting parameters d_B and θ_B , and n_L ; n_L indicates how far a tool (e.g., a needle) can extend outside the bronchoscope's working channel. (b) Bronchoscope's diagnostic FOV, given by θ_{FOV} and n_L . A route leading to ROI $\mathbf{R}$ is feasible if at destination $\mathbf{x}_D$, a point $\mathbf{x} \in \mathbf{R}$ satisfies (6–8).

Fig. 5.

Example displays pertaining to image-guided bronchoscopy. (a) Report inspection: Interactive movie viewer depicting a prebronchoscopy report for an eight-generation route of length 136 mm. The viewer gives pictorial views and quantitative airway-diameter and distance-to-ROI information along a route. (b) Live bronchoscopy: guidance-computer display during a live procedure. The 3-D Airway-Tree Viewer (left) gives a global view of the airway tree (brown), airway centerlines (red), and optimal route (blue) toward a target nodule (red). The yellow cylinder with green needle represents the bronchoscope tip's current position. The Endoluminal viewer (right) depicts two manifestations of the bronchoscopic video and complementary VB views. The top view simultaneously shows the live bronchoscopic video feed at the current position (left) and the next target VB view along the guidance route (right). The blue line again signifies the preplanned route and clearly indicates the next airway to enter. The bronchoscope currently resides in a generation-4 airway and has 26 mm to travel along the route to reach the target, per the display legend "Dist to ROI = 26 mm." The bottom portion of the Endoluminal Viewer represents a frozen "base camp" for the registered pair of views from the previously navigated generation-3 airway. The base camp serves as a fail-safe back-up point. Overall, for this case, the physician navigated an ultrathin bronchoscope eight airway generations toward the nodule and successfully collected samples via BAL and brushing (Case 20349-3-25). (a) Report inspection. (b) Live bronchoscopy.

Fig. 6.

Application of guidance strategy, Algorithm 3, during bronchoscopy on a phantom fabricated from the segmented airway tree of the case in Fig. 1 [39]. The figure illustrates system displays during a right-lung maneuver from a generation-2 airway to a generation-3 airway. Part (a) begins the process after completion of registration/fusion in the generation-2 right main bronchus (RMB). The panel shows a 3-D airway-tree rendering (brown) and the corresponding display in the Endoluminal Viewer, which simultaneously shows a fused version of the bronchoscopic video $I_{V+r}^{\Theta_2}$ (left view) and the registered fused VB view $I_{CT+r}^{\Theta_{v2}^o}$ (right view). This view can be saved as a synchronized “base camp” view for location Θ_{v2}^o . In all views, the blue line, which is the preplanned route $\mathbf{r}$, indicates the next airway to enter, while the red lines indicate other branches $\mathbf{b}_m \in \mathbf{r}$. In the airway-tree rendering, the yellow cylinder with green needle represents the bronchoscope tip’s current position within the airway tree. In part (b), the Endoluminal Viewer indicates the next location Θ_{v3} in the right intermediate bronchus (RIB) to navigate; the panel also shows the target ROI now $< \delta = 40$ mm from Θ_{v3} , as evidenced by the appearance of the ROI (green) and reference arrow (blue). Next, part (c) shows the resulting video view $I_V^{\Theta_3}$ after the physician maneuvers the bronchoscope close to the suggested location Θ_{v3} ; the 3-D airway-tree rendering shows the advancement via the yellow cylinder. Finally, part (d) depicts the result of registration/fusion; route and ROI information are fused with the video and VB views. (a) Base camp in the RMB at location Θ_{v2}^o . (b) Next VB view at location Θ_{v3} in RIB. (c) Bronchoscope moved close to VB view of (b). (d) After registration and data fusion.

Fig. 7.

Image-guided bronchoscopy for a 14-mm-diameter nodule in RB8. View (a) shows rendered 3-D airway tree, 13-generation guidance route (blue), centerlines (red), and nodule (red). Views (b–f) show registered pairs of bronchoscopic video and VB views displayed in the system’s Endoluminal Viewer at generations 5, 6, 10, 12 (penultimate airway), and 13 (final biopsy site); fusion information omitted on the video views for clarity. (We omit the generation-11 view, because navigation proceeded “straight ahead” from generations 10 to 12, and the generation-11 airway was only 15 mm long.) The generation-13 view vividly

illustrates the correspondence between the “real” bronchoscopic video, which clearly shows the nodule within the airway, and the corresponding registered VB view, which depicts the predefined rendered nodule (red) and localization arrow. (Case 20234-3-24; MDCT image specifications: $x = y = 0.62$ mm, $z = 0.5$ mm, 608 0.75-mm thick sections.) (a) Airway Tree. (b) Generation 5. (c) Generation 6. (d) Generation 10. (e) Generation 12. (f) Generation 13.

Fig. 8.

Example of a difficult maneuver due to a sharp branching angle. (a) Global airway tree rendering, where blue line represents preplanned route, target nodule in green, and arrow indicates the location of the difficult turn. (b) Close-up view of the airway tree near the LUL target site; yellow cylinder with green needle indicates current site. (c) Bronchoscopic video frame and corresponding VB view depicting the turn. The majority of the guidance time involved completing a single bronchoscope maneuver near this location. The physician had to insert the bronchoscope into a small orifice at an unusually sharp branching angle. As indicated by the blue line, the physician had to enter the top bronchus. The route was clear to the physician, but the maneuver required many attempts (Case 20349-3-25). (a) Airway tree. (b) Close-up view. (c) Endoluminal renderer.

TABLE I**Bronchoscopes Used in Our Studies**

Bronchoscope	d_B	Bending Angles	θ_{FOV}
Olympus XP160F ultrathin	2.8 mm	180° up, 130° down	120°
Olympus BF P180	4.9 mm	180° up, 130° down	120°
Pentax EB-1570K	5.5 mm	210° up, 130° down	120°

The bending angles help specify the maximum bending angle θ_B . The ultrathin bronchoscope has a 1.2-mm-diameter working channel, while the other bronchoscopes have a 2.0-mm-diameter working channel.

TABLE II

Ten-Case Retrospective MDCT-Based Study of Optimal Route Planning

	Device Constraints		Route Characteristics			
Case	d_B	θ_{FOV}	$\ x_D - R\ $	Branches	d_I	
1, 1, trial 1	2.8	180	38.0	9	2.9	
1, 1, trial 2	none	180	28.3	8	2.1	
1, 1, trial 3 [*]	2.8	70	69.6	6	6.1	
1, 2	2.8	70	16.9	9	4.1	
2, trial 1	2.8	180	36.4	6	3.0	
2, trial 2 [*]	2.8	70	46.3	5	3.0	
3, trial 1	2.8	180	34.7	5	3.6	
3, trial 2	none	70	32.0	6	2.4	
4, trial 1 [*]	2.8	180	42.4	5	3.3	
4, trial 2	none	180	29.2	8	1.5	
5	2.8	180	23.1	4	3.5	
6 ^{**}	2.8	70	4.7	6	2.8	
7 ^{**}	2.8	70	1.4	5	2.8	
8	2.8	70	24.4	6	2.8	
9	2.8	70	28.7	5	3.7	
10 ^{**}	2.8	70	1.0	9	2.9	

Unless otherwise specified, we used $nL = 40$ mm and assumed the use of an Olympus XP160F ultrathin bronchoscope (see Table I). The 'Case' entries refer to various trials; e.g., "1, 1, trial 1" refers to the first trial for case 1 and ROI 1. The quantities d_B , distance $\|x_D - R\|$, and d_I are in units mm, while θ_{FOV} is in degrees. With respect to the restrictions (4–7), the column $\|x_D - R\|$ indicates the distance of destination $\mathbf{v}_D$ from the ROI's surface for the optimal route, the column "branches" indicates the number of airway generations constituting the route (trachea = generation 1), and column d_I indicates the smallest diameter airway encountered along the route.

"**" indicates that the optimal route is > 40 mm from the target ROI (no feasible route), while

"***" indicates that the ROI is endoluminal.

TABLE III

Airway-Tree Characteristics for an 81-Case Database

Gen. (Cases)	Branches	Diameter	Length	Angle
2 (81)	162	15.6±2.6	40.7±16.5	42
a. RMB	81	17.0±2.4	26.1± 6.9	—
b. LMB	81	14.2±2.0	55.4± 5.9	—
3 (81)	322	12.0±2.1	17.4± 6.9	45
4 (81)	638	9.1±2.3	11.6± 9.3	44
5 (81)	1262	6.5±2.0	11.4±10.3	40
6 (81)	2374	4.7±1.4	13.6±10.1	39
7 (81)	3674	4.0±1.1	14.6± 9.7	38
8 (81)	4230	3.7±0.9	14.6±10.3	38
9 (79)	3261	3.6±0.8	14.1±10.9	39
10 (78)	2030	3.6±0.7	14.3±10.3	39
11 (69)	1254	3.6±0.7	15.4± 9.7	38
12 (64)	751	3.5±0.7	15.6±10.5	38
13 (49)	364	3.5±0.6	14.7±12.5	37

Column “Gen. (cases)” indicates airway generation index (trachea = generation 1) and the number of cases having 1 airway at the indicated generation. “Branches” enumerates the total number of airway branches found at a given generation over all 81 cases. Quantities “diameter” and “length” denote the mean values of the airway diameter d_j and airway length, with values given as mean $\pm$ S.D; units are mm. Right main bronchus (RMB) and left main bronchus (LMB) data are broken apart separately for the generation-2 measures. “Angle” indicates the mean branch angle θ_j in units degrees. Because the standard deviations of the branch angle measurements at each generation consistently ranged between 19 and 25, we omit S.D. For clarity. (One case arose from a Philips TrueFlight PET-CT scanner; image specifications: $x = y = 0.64$ mm, $z = 0.8$ mm, slice thickness = 1.0 mm, 631 1.0-mm thick sections.)

TABLE IV

Summary of Target ROI Sites

Site Type	RUL	RML	RLL	LUL	LLL	Total
Nodule (< 3 cm)	4	5	3	9	1	22
Mass (>3 cm)	0	1	0	3	0	4
Infiltrate	5	2	4	4	1	16
GGO	0	0	2	1	0	3
BAL Site	3	1	0	0	0	4
Lymph Node	3	1	1	2	0	7
Other	3	2	2	3	3	13
Total	18	12	12	22	5	69

Nodules > 3 cm in diameter were classified as a "mass." GGO = ground-glass opacity, BAL = bronchoalveolar lavage, "BAL Site" sites were defined as airway locations for performing BAL. "Lymph Node" refers to intrapulmonary lymph nodes. "Other" sites included seven sites examined via visual inspection only (no tissue sample taken), three cavitary lesions, one collapsed airway as seen on CT during procedure planning, one cavity wall, and one foreign body. The middle five columns refer to the locations of ROIs: RUL = right upper lobe, RML = right middle lobe, RLL = right lower lobe, LUL = left upper lobe, LLL = left lower lobe.

TABLE V

Planning and Guidance Summary Per Target ROI Type

Site Type	Number of Airways (Mean $\pm$ S.D.)			Bronchoscopes Used		
	Predicted Insertion Depth	Actual Insertion Depth	Ultrathin	Both	Large	Total
Nodule	6.8 $\pm$ 1.9	7.4 $\pm$ 2.5	14	4	4	22
Mass	5.8 $\pm$ 2.1	5.8 $\pm$ 2.1	0	2	2	4
Infiltrate	7.5 $\pm$ 2.3	6.9 $\pm$ 2.1	13	0	3	16
GGO	10.7 $\pm$ 1.5	9.0 $\pm$ 1.7	3	0	0	3
BAL site	7.7 $\pm$ 1.5	7.3 $\pm$ 1.7	4	0	0	4
Lymph Node	5.4 $\pm$ 1.1	4.4 $\pm$ 1.3	0	1	6	7
Other	8.6 $\pm$ 2.2	8.2 $\pm$ 2.1	11	1	1	13
Total	7.3 $\pm$ 2.3	7.1 $\pm$ 2.4	45	8	16	69

Ultrathin = targets examined with an ultrathin bronchoscope only; Both = targets examined with both the ultrathin bronchoscope and a large bronchoscope; Large = targets examined with a large bronchoscope only.

TABLE VI

Planning and Guidance Summary Broken Down by Processing Stage

	Number of Airways			Terminal Airway Diameter		
	Mean	Median	Range	Mean	Median	Range
Stage 1: 3D MDCT Analysis						
Predicted Insertion Depth						
All target sites (n=69)	7.3±2.3	7	4–12	3.9±1.5	3.2	2.4–9.0
Ultrathin bronchoscopy only (n=45)	8.2±2.1	8	5–12	3.2±0.5	3.1	2.4–4.6
Two bronchoscopes used (n=8)	6.9±1.6	7	4–9	3.4±1.4	2.9	2.7–6.7
Large bronchoscope only (n=16)	5.1±0.9	5	4–7	6.2±1.4	5.7	4.6–9.0
Stage 2: Guided Bronchoscopy						
Actual Insertion Depth						
All target sites	7.1±2.4	7	3–13	4.3±2.1	3.7	2.3–11
Ultrathin bronchoscopy only	8.0±2.0	8	4–13	3.6±1.5	3.1	2.4–10
Two bronchoscopes used	6.9±2.3	7	4–10	3.7±1.5	3.4	2.3–6.7
Large bronchoscope only	4.7±1.4	4	3–8	6.6±2.3	6.0	3.8–11

Results presented as Mean ± S.D. unless otherwise indicated. "Number of airways" = number of airways traversed by a route toward a target site (trachea = 1). Predicted bronchoscope insertion depths for the "two bronchoscope" sites were based on the ultrathin bronchoscope being the primary device. Terminating airway diameter (mm) is defined as follows: for Stage 1, diameter of final airway predicted to be navigable for a chosen bronchoscope; for Stage 2, diameter of final airway reached by physician during bronchoscopy.

TABLE VII

Navigation Success Results

		New System				Shinagawa <i>et al.</i> (ultrathin only)			
		All Sites		Ultrathin only					
Lobe	No.	Depth	No.	Depth	No.	Depth	No.	Depth	Significance
RUL	17	6.0±1.8	11	7.0±1.3	20	5.0±1.3			$p=0.0003$
RML	11	7.8±1.9	6	8.3±1.5	7	6.9±0.9			$p=0.0618$
RLL	11	9.4±2.6	8	10.3±2.1	23	5.9±1.3			$p<0.0001$
LUL	21	6.9±2.3	13	8.2±1.8	21	5.4±1.3			$p<0.0001$
LLL	3	7.3±0.6	2	7.5±0.7	14	6.1±1.4			$p=0.1954$
Total	63	7.3±2.4	40	8.3±1.9	85	5.7±1.3			$p<0.0001$

The table also compares the actual bronchoscope insertion depths of our system and a system tested by Shinagawa *et al.* "New System" refers to the image-guided bronchoscopy results achieved with our system for the 63 of 69 correctly navigated target sites; the "ultrathin only" column focuses on the subset of 40 of 45 sites correctly navigated using the ultrathin bronchoscope. "Shinagawa *et al.*" refers to the results reported in VB-guided ultrathin bronchoscopy study of Shinagawa *et al.* [23]. "No." equals the number of target ROIs for a given situation. "Depth" equals the mean actual bronchoscope insertion depth (Mean $\pm$ S.D.). "Significance" (column 8) compares the ultrathin-only results of our system (column 5) and Shinagawa *et al.* (column 7); statistical significance was determined using the two-tailed version of the Student's *t*-test.