Objective measurements of central airway stenosis. A pilot study.

Debora Gil, PhD[1,2,3], Rosa Maria Ortiz, MD [1,4], Carles Sánchez, PhD[1], and Antoni Rosell, MD, PhD[4,5,6,7] on behalf of the SENSA team*

This research was carried out at Hospital Universitari Bellvitge and Computer Science Department, Barcelona, Spain.

[1]Computer Vision Center, Bellaterra, Barcelona, Spain

[2] Computer. Science Department, UAB, Bellaterra, Barcelona, Spain.

[3] Serra Hunter Fellow.

[4]Department of Respiratory Medicine, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain.

[5]Institut d'Investigació Biomedica de Bellvitge (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain.

[6] CIBER de Enfermedades Respiratorias (CIBERES), Bunyola, Mallorca, Spain.

[7]Universitat de Barcelona (UB) Facultad de Medicina, Barcelona, Spain.

Short title: Real-time computing Stenosis Index

Corresponding author: Rosa Maria Ortiz-Comino. Centro de Vision por Computación. Campus UAB, Edifici O, s/n, 08193 Cerdanyola del Vallès, Barcelona..

Phone: +34 93 581 18 28   Fax: +34 93 581 16 70   rm.ortizcomino@gmail.com

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ABSTRACT

Background: Subjective estimation of degree of stenosis in central airway obstruction is highly variable.

Objective: This paper aims to determine the benefits of using SENSA (Software for Endoscopic Stenosis Assessment) for obtaining an accurate Stenosis Index (SI) measurement in a group of experts and non-expert pulmonologists.

Methods: SI obtained by pulmonologists and SENSA were compared with a reference SI to set their precision in SI computation. We used SENSA to efficiently obtain this reference SI in 12 selected cases of benign stenosis. 7 interventional and 7 general pulmonologists were enrolled to validate SENSA usage. A web platform with three user-friendly micro-tasks was designed to gather data. Users had to visually estimate the Stenosis Index (SI) from videos with and without contours of the normal and obstructed area provided by SENSA. Besides users were able to modify SENSA contours to define the reference SI.

Results: SI visual estimation accuracy was not associated with either the level of expertise ($p=0.75$) nor the contours of the normal and obstructed area provided ($p=0.43$). SENSA SI precision confidence interval (CI) was 95.4% - 99.2% which is significantly better than visual estimation SI precision ($p<0.001$), with at least 26% of improvement. There was a tendency toward increased SENSA SI precision when computing severe versus moderate stenosis.

Conclusion: SENSA provides objective SI measurement with a precision of up to 99.5%

that can be calculated from any bronchoscopes using an affordable scalable interface. Providing normal and obstructed contours on bronchoscopic videos does not improve pulmonologist SI visual estimation.

1. INTRODUCTION

Central airway obstruction (CAO) is a clinical condition in which the main airway diameter is reduced. CAO impact on patients' symptoms and functional status depends on the degree of stenosis, among other variables such as type, structure or location, included in the proposed classification by Freitag et al [1]. The objective quantification of the degree of obstruction would be desirable to talk about the severity of the stenosis, as well as for monitoring progression and response to treatment. Spirometry, Computed Tomography and Morphometric Bronchoscopy are among the techniques available for the objective assessment of actual airway calibre [2,3,4,5].

In clinical practice, airway calibre is usually assessed visually during bronchoscopy procedures [6]. This subjective assessment is dependent on multiple variables during examination and on the wide angle lens of the bronchoscope. Murgu et al showed that subjective assessment does not correlate with the number of procedures performed by the bronchoscopist, who can either underestimate or overestimate the degree of stenosis [7]. Morphometric analysis bronchoscopy (MB) quantifies stenosis using the Stenosis Index (SI) which is calculated from the cross-sectional area (CSA) of the airway. SI represents the CSA of the obstructed airway to that of a normal airway proximal or distal to the stenosis [8]. MB calculates CSA using cost-free image processing software to manually select the contours that define each CSA. Although it has been reported that MB provides reliable measurements, a main limitation is the manual intervention in CSA computation, which discards its use during the procedure. Bronchoscopists highlight the need for an accurate and precise method for the quantification of SI [6] but they ask for more convenient and rapid methods than the actual software. To date, no real-time acquisition and processing systems for calculating SI are available.

As an alternative to MB, the authors developed a software named SENSA (Endoscopic Stenosis Assessment), which computes SI with CSA contours automatically extracted by the system from the analysis of video frames [9]. SENSA can calculate SI in less than 10 seconds by analysing standard bronchoscopic data without the need for other imaging technologies. According to a previous pilot off-line study, SENSA SI accuracy was around 9% of error.

The goal of this paper is to determine the benefits of using SENSA for obtaining a more efficient and accurate SI in a group of experts and non-expert pulmonologists.

2. METHODOLOGY

2.1. Study design

Bronchoscopic videos were obtained from patients with benign CAO at the Respiratory Endoscopic Unit of Hospital Universitari Bellvitge. In each video, the proximal view of the tracheal stenosis and distal normal airway were visualized. Videos were recorded using an Olympus BF P160 and BF T180 videobronchoscopes (Olympus Corp, Tokyo, Japan)

A first sequence from each video was chosen in which the scope was seen proximal to stenotic area, moving inside the stenotic area and crossing it to show the distal lumen. Two more sequences, lasting three seconds each, were compiled from each video, one from a healthy anatomy and one from the obstructed one, in which the videobronchoscope was positioned 1cm proximal to each area. These three seconds were converted into frames and were processed by SENSA, outlining the trachea/bronchi contours. Frames showing healthy and obstructed segments with SENSA contours drawn in two different colours (white for healthy, red for obstructed) were displayed in two different windows. One of the authors browsed through the healthy sequence as well as through the stenotic one using a slide bar to select the frames best suited for stenosis computation.

A total number of 14 pulmonologists (seven interventional and seven general pulmonologists) from four different University Hospitals were enrolled to validate SENSA usage. The criteria applied for the classification as an Interventional or general pulmonologist was based on the number of bronchoscopies performed. The former had performed over 1000 bronchoscopies in their lifetime while the later had performed fewer than 200 bronchoscopies.

2.2. Validation

Under the assumption that MB provides a reference SI value[1], the SI obtained by pulmonologists and SENSA were compared to this reference to set their precision in CAO computation. Precision was normalized in percentage ranges [0%, 100%], with

100% being the maximum possible precision. In this study we used SENSA to efficiently obtain MB reference SI. Since SENSA SI computation depends exclusively on the precision of computed CSA contours, SENSA contours were shown to pulmonologists for their manual correction. The SI obtained from SENSA corrected contours was considered our MB reference for assessing SI precision. Given that more than one contour was drawn for each case (one per physician), the reference value was defined from CSA obtained from the consensus of all experts' annotations [10,11]. We also stored the time needed to correct contours to set SENSA as a tool for efficient MB.

The following validation aspects were considered:

Precision in Visual SI. Pulmonologists were required to estimate SI through the visual inspection of exploration videos firstly without any processing and secondly by displaying SENSA contours to support their visual assessment. Precision in experts' SI was compared according to their expertise.

Precision in SENSA SI. SENSA precision was compared to the precision of the best and worst visual estimation in the study. Since airflow resistance decay is inversely proportional to SI, SENSA precision against different stenotic degrees was also analysed to detect whether it increased with stenosis severity. Severity was classified according to the reference SI as moderate-mild <75% and severe >75% [12].

To collect the data for SENSA validation, we defined three user-friendly micro-tasks [10] (see Fig.1), which are available on-line [13].

1) Visual SI. The videos showing the proximal view of the stenosis and moving into it were shown to users, who could stop and replay them as many times as they liked. Pulmonologists were asked to visually estimate SI and write it down in a textbox.

2) Visual SI using SENSA contours. SENSA CSA contours displayed on the frames selected by the expert were shown to users for visual SI estimation. To allow for an easier comparison of stenotic and healthy CSA, an image displaying both contours on the obstructed frame was also provided. As before, pulmonologists were asked to write the estimated SI in a textbox.

3) Manual edition of SENSA contours. The frames of the previous task were shown to pulmonologists for the correction of CSA contours by clicking image points on the right contour every time SENSA CSA was considered to be sub-optimal. In order to make manual edition efficient, we used a computational algorithm that allowed for corrections using a minimal set of points.

The web platform for data gathering followed a client-server architecture with a web page for remote access to the micro-tasks that stored all data in a central server installed at the Computer Vision Center. The website was created by combining html with programming languages like php and javascript. The pulmonologists enrolled in the study were provided with a user ID and password for a secure log in to the validation webpage. A short manual was designed to guide physicians through each task. Once pulmonologists had logged in, they chose the case they wanted to validate from the cases they had not validated yet. After ending a case (the three micro-tasks), SI, time and corrected points were stored in the central server and the case was removed from the to-do-list shown at the log-in site.

2.3 Statistical Analysis

Precision and time were the variables used in this statistical analysis. Descriptive statistical analysis was carried out for all variables in the study, using number of samples, mean and standard deviation (sd). Main analyses were performed using a mixed model considering patient and pulmonologist as random factors. Model assumptions were validated by means of residuals analysis. For each model, we computed model parameters, p-values for significance in main effects and CI for their mean values.

For assessment of visual SI precision, we adjusted a random effects model with pulmonologist expertise, information about CSA contours provided and its interaction as fixed effects. For assessment of SENSA SI precision, SENSA was considered as a new observer with expertise label “SENSA” in a random effect generalized model with expertise as fixed effect. Finally, we also adjusted a logarithmic model with stenosis severity as fixed effect to assess SENSA performance across lesion severity. Significance level was set to <0,05 and analyses were conducted using R, version 3.3.3 [14].

3. RESULTS

A total of 12 cases were downloaded for validation in the webpage (Table 1). 14 pulmonologist (seven interventional or expert and seven general or non-expert pulmonologists) completed the three microtasks for each case.

The analysis of visual SI precision (summarized in Table 2), did not detect any significant interaction between pulmonologist expertise and information about contours (p= 0.85) nor across groups (p= 0.43 for information provided and p= 0.75 for degree of expertise). Confidence Intervals (CIs) for visual SI precision were 63.7% - 79.1% for interventional and 61.3% - 77.6% for general pulmonologist.

According to the model (summarized in Table 3), differences in SI precision between SENSA and pulmonologists are significant ($p<0.001$). CI for SENSA SI precision was 95.4% - 99.2%. SENSA increases precision by 24.6% on average with respect visual estimation (Fig2). Analysis of SENSA SI according to stenosis severity (Fig.3) presented a tendency towards an increase in SENSA precision for severe cases, though differences were not statistically significant (p= 0.21).

Finally, CI for the time required to obtain a reference SI by correcting SENSA contours was 30.77-42.34 seconds. No differences between experts and non-expert pulmonologist (p=0.36) were found.

4. DISCUSSION

The results of this study demonstrate: 1) The precision in the estimation of SI is similar between interventional and general pulmonologists. 2) The accuracy of visual evaluation does not improve with obstructed and normal contours superimposed on bronchoscopic images. 3) SENSA provides precise and reliable objective SI measurements without manual intervention. 4) SENSA is especially accurate when computing severe CAO.

It is well known that a high inter-observer variability exist regarding visual SI estimation and that experience does not correlate with a more accurate estimation[8]. This study corroborates the idea that interventional and general pulmonologists provide similar SI values when asked to calculate SI. Furthermore, it was hypothesized that bronchoscopic images with superimposed normal and obstructed contours might improve the accuracy of visual estimations. However, when results were analysed, no significant improvement was observed and physicians were still far from achieving an objective SI measurement. It is likely that visual SI estimation cannot be improved without exhaustive training due to the limitations of the human perception of distances and measurements [15]. Physicians already achieve maximum precision without superimposed contours and thus, providing tools that support the visual estimation of CAO are not helpful.

To the best of our knowledge, SENSA is the first tool that allows for SI computing without manual intervention. Manual corrections are not necessary but users can undertake them if desired. Similarly to MB, the SI computed from SENSA corrected contours was used as our reference standard [8]. This study shows that SENSA SI precision is 95.4% - 99.2%. Precision is above 95% in 10/12 (83%) cases and rises to 99.5% in 5/12 cases. Only in Case 4 and Case 6 did SENSA error increase and precision drop to 90% (Case 4). In every case, SENSA proved to be superior to visual estimation, with an improvement of 26%.

Since CAO clinical impact varies based on the degree of stenosis, but also on the typology or baseline status of the patient [16], it would interesting to know if there are clinical consequences of a 5% increment in SI, which is the expected maximum error achieved by SENSA. Until then, SENSA allows for easy manual correction, in 30 seconds on average, using a web application supported by any portable device.

Furthermore, this study examined the accuracy of SENSA SI measurement with regard to the degree of stenosis. SENSA variation decreases with the severity of stenosis, with a precision of up to 99% in five out of seven cases of severe stenosis. These findings are relevant in patient care because patients with severe stenosis require clinically relevant decisions with a faster intervention given the higher risk of early and severe complications. This study demonstrates that SENSA can be trusted to provide an exact SI, so a treatment approach can be accurately decided. Moreover, SENSA is a radiation-free and user-friendly software that does not require a learning process and provides data that can be stored and shared easily. Besides, SENSA can be easily deployed in bronchoscopy suites using a client-server architecture (similar to the validation website) and cloud computing.

There are a few limitations to this study that need to be addressed. Firstly, SENSA corrected contours were used as standard to compute a reference SI because there is no available gold standard. The absence of such a reference standard is a common limitation for validating image processing procedures [11]. Like crowdsourcing approaches, our reference standard is determined by the consensus of all experts' annotations [10] which, in our case, correspond to the intersection of SENSA corrected contours. For complex obstructions with large inter-observer variability, such a consensus may overestimate SI and introduce an apparent decrease in precision (Case 4 and Case 6).

Secondly, this study shows that SENSA is able to outline with accuracy CSA contours and thus, compute an accurate SI from them. However, frames provided to SENSA to compute CSA are selected from bronchoscopy videos by users. This introduces a certain degree of subjectivity into the computations. We are working on the incorporation of new tools that will allow SENSA to measure distances during the acquisition and therefore select frames at equal distances for the computation of obstructed and reference CSA contours [17].

Thirdly, we are aware that the small number of cases and users in which it has been tested limits the generalizability of these results. We are aiming to recruit a larger sample of cases, using the new tools that are being developed and to complete a formal international evaluation.

Finally, we are aware that CAO involves other parameters that we are not taking into account such as stenosis morphology, location or typology. There is no recognized classification scheme for CAO but the proposal published by Freitag et al 10 years ago [1]. We are confident that objective measurement of degree of stenosis with SENSA could can be a valuable tool involves in a possible standardized classification for CAO such as the one mentioned.

In conclusion, SENSA is a genuine software package that represents the first step towards quasi-real time SI measurement and that works in commercial bronchoscopes without altering intervention protocol and, last but not least, is an affordable scalable interface since its implementation only requires internet access.

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Table 1. Aetiology, location, morphology and stenosis index/degree of narrowing for the 12 strictures analysed

Case	Age	Sex	Type of benign stenosis	Location of stenosis	Stricture morphology	Reference SI (%)
1	63	M	PITS	TRACHEA (Upper 1/3)	Circumferential	76.9
2	51	F	PITS	TRACHEA (Upper 1/3)	Circumferential	91.5
3	71	F	PITS	TRACHEA (Upper 1/3)	Circumferential	71.0
4	75	F	PTTS	TRACHEA (Upper 1/3)	Triangular	34.6
5	75	F	EDAC	LMB	Elliptical	70.2
6	69	F	TRACHEO-BRONCHOPATHIA OSTEO-CHONDROPLASTICA	TRACHEA (Lower 1/3)	Elliptical	52.1
7	63	M	PITS	TRACHEA (Upper 1/3)	Circumferential	58.3
8	81	F	PITS	TRACHEA (Upper 1/3)	Circumferential	94.9
9	68	M	EDAC	LMB	Elliptical	88.8
10	59	M	PTTS	TRACHEA (Upper 1/3)	Triangular	75.1
11	76	F	PITS	TRACHEA (Upper 1/3)	Circumferential	78.0
12	64	M	PITS	TRACHEA (Upper 1/3)	Hourglass	83.15

SI: Stenosis Index. PITS: Post Intubation Tracheal Stenosis. PTTS: Post-Tracheostomy Tracheal Stenosis. EDAC: Excessive Dynamic Airway Collapse. LMB: Left main bronchus

Table2: Precision in Visual SI		Descriptive			Model		
Explicative Variables		n	mean	sd	Coeffi-cient	p-value	CI 95%
Expertise	Interventional	168	71.82	17.67	1	--	(63.7,79.1)
	General	144	69.64	19.36	-1.57	0.75	(61.3,77.6)
Information	None (Visual Assessment)	156	69.28	19.72	1	--	(63.1,76.3)
	CSA Contours (SENSA Assisted)	156	72.35	17.05	1.88	0.433	(64.6,77.8)

SI: Stenosis Index. CSA: Cross Sectional Area

Table3: Precision in SENSA SI		Descriptive			Model		
Explicative Variables		n	mean	sd	Coeficient	p-value	CI 95%
Stenosis Severity	Severe (>75%)	7	98.2	2.3	1	--	(99.2,101.6)
	Moderate (<75%)	5	95.0	5.2	1.2	0.21	(97.8,100.6)
Calculation	SENSA	12	96.9	3.9	-2.3	<.0001	(95.4,99.2)
	Interventional	12	83.9	13.3	1	--	(64.7,80.6)
	General	12	57.9	11.3	.03	0.87	(63.3,80.4)

SI: Stenosis Index

Figure 1: Webpage validation tasks. White : normal contour outlined by SENSA; Red: obstructed countour outlined by SENSA. White dots: users corrections for normal contours, Red dots: users corrections for obstructed contours.

Figure 2: Comparison of Stenosis Index Precision (%) between SENSA and Best and Worst Visual Estimation

Figure 3: SENSA SI Precision (%) across Central Airway Obstruction Severity.