Do Current Lung Cancer Screening Guidelines Apply for Populations With High Prevalence of Granulomatous Disease? Results From the First Brazilian Lung Cancer Screening Trial (BRELT1)

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Background. Low-dose computed tomography (LDCT) screening for lung cancer has been demonstrated to be effective in reducing cancer mortality. However, these studies have not been undertaken in countries where the incidence of granulomatous disease is high. The First Brazilian Lung Cancer Screening Trial (BRELT1) has completed initial accrual and is now in the follow-up phase. We present results from the initial prevalence round of screening.

Methods. The inclusion criteria were the same as those for the National Lung Cancer Screening Trial (NLST). Pulmonary nodules larger than 4 mm were considered positive and required evaluation by a multidisciplinary team. Indeterminate nodules were evaluated with fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) or biopsy when indicated. Statistical analysis was performed with Fisher's exact test to compare our positive findings with those of the NLST.

Results. From January 2013 to July 2014, 790 participants were enrolled. Positive LDCT scans were reported in 312 (39.4%) participants, with a total of 552 nodules larger than 4 mm. The comparison between positive findings in the NLST (7,191 of 26,722 cases) and those in the BRELT1 (312 of 790 cases) showed a significant difference ($p < 0.001$). The positive predictive value was lower in BRELT1 than in the NLST (3.2% versus 3.8%, respectively). Follow-up imaging was indicated in 278 of 312 (89.1%) participants; 35 procedures were performed in 25 participants. In 15 cases, benign lesions were diagnosed. Non–small-cell lung cancer (NSCLC) was diagnosed in 10 patients (prevalence of 1.3%). In 8 patients (stage IA/IB disease), treatment was by resection only, in 1 patient neoadjuvant chemotherapy was used (stage IIIA), and in 1 patient advanced disease was diagnosed (stage IV).

Conclusions. Using NSLT criteria, a larger number of patients had positive scans (nodules), compared with previous lung cancer screening studies. However, the number of participants requiring surgical biopsy procedures and who were ultimately identified as having cancer was similar to other reports. This supports the role of screening in patient populations with a high incidence of granulomatous inflammation.

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Lung cancer has a high incidence in Brazil; approximately 34,000 new cases are diagnosed each year [1]. Advances in treatment have been made, but the long-term survival rate of patients diagnosed with primary lung cancer malignancies remains low [2, 3]. Lung cancer is often diagnosed at an advanced stage; only 15% of patients are diagnosed with early-stage disease. If diagnosed when the disease is still localized, the 5-year survival rate is about 55% to 60%, compared with 4% for patients with advanced-stage disease [4].

Smoking as a risk factor for lung cancer has been established for more than 50 years [2–4]. Although the rate of smoking has declined in Brazil in the past few

years, a large number of current or former smokers remain at elevated risk for this malignancy [5].

Early detection in lung cancer is an important tool for decreasing mortality. During the past decade, the availability of low-dose computed tomography (LDCT) has facilitated interest in lung cancer screening [6]. The published results of the National Lung Screening Trial (NLST) demonstrated that LDCT screening for lung cancer provided a 20% relative reduction in mortality rates among individuals at high risk [7]. In addition, studies regarding lung cancer screening showed that the disease could be detected in early stages in more than 80% of cases [8–16]. Others studies are still being conducted around the world to evaluate the mortality reduction and the cost-effectiveness of lung cancer screening programs.

Despite these results, lung cancer screening is not established as a public health practice, and this issue still generates controversy, especially in developing countries such as Brazil, where there are high rates of granulomatous disease such as tuberculosis [17]. In Brazil, despite the reduction in the incidence of tuberculosis by more than 50% in the past 2 decades, there are still areas with a high incidence of the disease [18].

The great majority of the studies on screening for lung cancer are from countries where the incidence of tuberculosis is smaller, with less than 10 cases per 100,000 inhabitants [17, 19]. Countries like Brazil, India, China, and Russia have an incidence of tuberculosis that is 5 to 10 times higher [17]. To date, there have been no studies of LDCT screening for lung cancer in such countries. This raises questions regarding the applicability of LDCT screening, because many pulmonary nodules may ultimately have an inflammatory cause.

Therefore we developed a lung cancer screening trial in the hopes of addressing the effectiveness of screening in relation to the Brazilian population.

The aim of this article is to present the results of the prevalence round of the First Brazilian Lung Cancer Screening Trial (BRELT1).

Patients and Methods

This was a single-center study that received federal funding. The study was approved by the Institutional Review Board of Hospital Israelita Albert Einstein. All participants signed an informed consent form. The primary outcome measure was the prevalence of lung cancer, and the secondary outcome was the prevalence of lung nodules deemed to be positive for cancer on LDCT, which ultimately were found to be benign.

From January 2013 to July 2014, 790 participants entered the program. They volunteered for the study in response to public calls in communication vehicles in the greater metropolitan area of São Paulo and by other community care services, including smoking cessation programs and labor unions.

The inclusion criteria were similar to those of the NLST [7] as follows: absence of significant respiratory symptoms, 55 to 74 years of age, current smokers with at least 30 pack-years' tobacco exposure or former smokers who quit within the past 15 years, and written informed consent obtained. The exclusion criteria included being unable to undergo CT, being pregnant, having previously undergone radiation therapy to the chest, and having severe comorbid disease, such as cardiovascular disease, lung disease, liver disease, kidney disease, or metabolic disease.

At the initial visit, demographic and smoking history data were collected for each individual. At the end of this visit, eligible participants were referred for LDCT. Furthermore, at this visit, current smokers were referred to a smoking cessation program.

All LDCT scans were obtained on a 64-row multidetector CT scanner (Toshiba Aquilion 64, Toshiba Medical Systems, Tokyo, Japan) using a low-dose technique, 120 kV, and 15 mAs maximum, using the adaptive iterative dose reduction feature. The images were reconstructed with collimation of 1×1 mm and stored on picture archiving and communication system (PACS) in Digital Imaging and Communications in Medicine (DICOM) format.

LDCT scans were analyzed by 2 board-certified radiologists with blinded interpretation, and the cases of disagreement were discussed. The report by the radiologist included the reader findings (location, size, demarcation, shape, and density [classified as solid, semisolid, or ground-glass opacity]) and recommendations for follow-up. The size evaluation was based on linear measurement of the greatest diameter in axial slices, and volume nodules were calculated by Philips nodule evaluation semiautomated software.

LDCT scans with indeterminate pulmonary nodules greater than 4 mm were considered positive. This is similar to the original NSLT criteria. Scans were evaluated by a medical team comprising radiologists, pulmonologists, and thoracic surgeons, who decided on follow-up strategy according to the established protocol for the first LDCT round (Table 1). Annual follow-up was recommended to participants with negative LDCT scans.

For the LDCT scans with solid nodules larger than 8 mm, the pretest probability of malignancy was also

Table 1. Decision Protocol for the First LDCT Round

Size	Solid Nodules
>4 mm and ≤6 mm	Follow-up LDCT in 6 mo
>6 mm and ≤8 mm	Follow-up LDCT in 3 mo
>8 mm	Calculate pretest probability:
	Low (<6%): follow-up LDCT in 3 or 6 mo
	Intermediate (6%–60%): PET/CT
	High (>60%): biopsy or surgical resection
	GGO or Partially Solid Node
Pure GGO ≤5 mm	Annual follow-up
Pure GGO >5 mm	Follow-up LDCT in 3 mo
Partially solid node	Follow-up LDCT in 3 mo

GGO = ground-glass opacity;   LDCT = low-dose computed tomography.

calculated based on the multivariate logistic regression model developed at Mayo Clinic [6].

Selected patients with indeterminate nodules were evaluated with fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT). When biopsy was indicated, procedures performed included bronchoscopy, transthoracic needle aspiration biopsy, endobronchial ultrasonography or video-assisted thoracic surgery (VATS). Resected tumors and specimens were analyzed by 1 pathologist.

After diagnostic confirmation and surgical treatment (when appropriate), patients were referred for oncologic follow-up. Participants with clinically significant incidental findings outside the lungs were referred to public or private health care services.

In this study, the positive screen rate was calculated as the number of patients with positive test results divided by the number of individuals screened. Also, for this analysis, false-positive cases were defined as those with no indication for an invasive procedure within the study period or those who had a negative biopsy result. Therefore the positive predictive value (PPV) was considered to be the number of true positive cases (those who were confirmed to have screen-detected lung cancer in this screening round) divided by the number of individuals with positive LDCT screens in the T0 round (true-positive + false-positive cases).

For the purpose of this article, NLST may represent a group of patients with a low incidence of granulomatous disease and BRELT1 is considered a group with a high incidence of granulomatous disease. Additional statistical analysis was performed with Fisher's exact test to compare the BRELT1 positive test results with those from the NLST.

Results

From January 2013 to July 2014, 4,030 individuals applied for the screening program. Of these individuals, 3,166 were not included because they did not meet the inclusion criteria. The most common causes for noneligibility were inadequate age or insufficient exposure to cigarette smoking. The remaining 864 individuals were included in

the protocol after signing the informed consent form. At completion of recruitment, 74 (8.6%) of the group dropped out, all because of refusal after the first agreement. Consequently, 790 participants underwent the baseline LDCT scan.

Women represented 50.1% (396 participants) of the sample. The mean age was 61.9 years (SD, 4.6). The proportion of current smokers was 55.2% (436 participants). The median packs per year was 53.6 (SD, 19.8). The mean duration of smoking cessation for the former smokers was 6.8 years (SD, 2.2).

At baseline LDCT, about 4,000 nodules were found in 790 participants; in 19 participants nodules smaller than 4 mm were too numerous to count (> 30). Nevertheless most of these nodules did not require further diagnostic workup because the size was less than 4 mm.

We found 312 positive LDCT scans at baseline (positive screen rate of 39.5% [312 of 790), with a total of 552 nodules larger than 4 mm. Among these 312 participants, 30 (9.6%) had a solitary nodule, 116 (37.2%) had 2 to 4 nodules, 91 (29.2%) had 5 to 9 nodules, and 75 (24%) had 10 or more nodules. The mean number of nodules per patient was 4.8 (SD, 6.2). The highest number of nodules identified in 1 patient was 47.

As mentioned previously, measured nodules larger than 4 mm were considered screen positive. Nevertheless, after this study was initiated, new international data suggested a new cutoff size of 6 mm to consider a nodule positive. In this T0 round, nodules 6 mm or larger were found in 145 participants, corresponding to a positive screen rate of 18.4% (145 of 790 cases) using this more limited criteria.

The comparison between positive findings in the NLST (7,191 of 26,722 [26%]) and BRELT1 (312 of 790 [39.5%]) showed a significant difference ($p < 0.001$). However, the number of lung cancer cases identified in both populations (1.0% versus 1.3%) was similar. The PPV for LDCT was lower in BRELT 1 than in NLST (3.2% versus 3.8%, respectively).

The distribution of participants according to the major nodule's size is showed in Table 2. Based on the radiologic appearance of the nodules, follow-up in 3 or 6 months was indicated in 97 (31.0%) and 182 (58.7%)

Table 2. Distribution According to the Major Nodule's Size, Lung Cancer Prevalence and Approach Based on 312 Positive Studies in 790 Participants

Nodule Size	n (%)	LDCT (3–6 mo)	PET/CT	Biopsy	Lung Cancer
4 to <6 mm	167 (21.1)	166	1	1[a]	. . .
6 to <8 mm	72 (9.1)	70	2	2	2
8 to <10 mm	28 (3.6)	21	5	2	1
10 to <20 mm	39 (4.9)	20	11	13	5
20 to <30 mm	4 (0.5)	1[b]	. . .	2	1
>30 mm	2 (0.3)	. . .	. . .	2[c]	1
Mediastinal/other	3 (0.4)[d]	. . .	. . .	3	. . .
Total	312/790 (39.5)	278/312 (89.1%)	19/312 (6.1%)	25/312 (8%)	10/312 (3.2)

[a] Endobronchial nodule.   [b] Nodule with benign calcifications (scar tissue)—stable after 1-y follow-up.   [c] Stage IV disease diagnosed with abdominal metastatic disease/cavitated lesion (tuberculosis).   [d] Mediastinal lesions (not counted as lung nodules).

LDCT = low-dose computed tomography;   PET/CT = positron emission tomography/computed tomography.

Fig 1. (A and B) Low-dose computed tomography (LDCT) sections show 11-mm solid nodule in left upper lobe with smooth borders and no evidence of calcification. (C) Sagittal reformation demonstrates posterior location of nodule in lobe close to fissure. Patient preferred operation, and histoplasmoma was diagnosed after wedge resection.
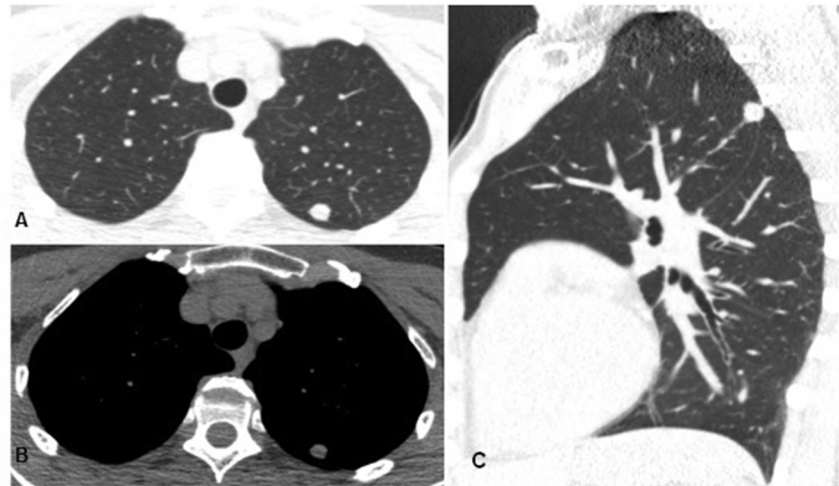
participants, respectively. The other cases required further investigation with PET/CT or lung biopsy. After multidisciplinary discussion, PET/CT was indicated in 18 participants and biopsy in 25 participants.

Among the 18 patients who underwent PET/CT, 6 had positive results (standard uptake value >2.5 or suspicion of malignancy based on nodule's morphologic appearance, or both). Biopsy was performed in these cases, diagnosing lung cancer in 5 participants and granuloma in 1 participant. Also, in 1 other case, a nodule grew between the first LDCT and the PET/CT, despite the morphologic features suggesting benign disease. Biopsy was subsequently performed and confirmed that the nodule was benign. After 6 months of follow-up, all negative PET/CT nodules were still stable, including 7 patients with lung nodules greater than 1 cm, for which PET/CT avoided invasive diagnostic tests.

A total of 35 minimally invasive procedures were performed in 25 participants. These included 14 image-guided biopsies (40%), 7 bronchoscopies (20%), 2 cases of endobronchial ultrasonography (6%), and 12 cases of VATS (34%). The mean length of stay in the hospital for the surgical patients was 3.8 days (SD, 1.8) with no mortality.

In 15 cases, benign lesions were diagnosed after biopsy (Fig 1). Three of these patients underwent minimally invasive surgical procedures because of the lesion size or type: 2 VATS wedge resections and 1 robotic mediastinal tumor resection (schwannoma). Granulomatous diseases were found in 10 participants, including 2 cases of tuberculosis. Besides the 2 cases of tuberculosis diagnosed with biopsy and bronchoalveolar lavage, 1 patient was additionally diagnosed by sputum analysis. All 3 participants received specific treatment.

Non–small-cell lung cancer (NSCLC) was diagnosed in 10 patients, corresponding to a prevalence of 1.3% (10 of 790 participants) and a PPV of 3.2% in the first screening round. In 8 cases (stages I A or I B), treatment was surgical only (Fig 2), but in 1 case (stage IIIA) neoadjuvant chemotherapy was prescribed, followed by

a surgical procedure. Moreover, in 1 patient, advanced disease was diagnosed (stage IV); interestingly, this participant had radiologic imaging 2 years previously, which found a lung nodule at the same location. Unfortunately he decided not to follow initial medical recommendations.

The surgical procedures for cancer patients were minimally invasive (VATS lobectomies) in 8 cases and thoracotomy with bilobectomy in the patient with stage IIIA disease who received neoadjuvant therapy. Histologic findings for cancers included invasive adenocarcinoma (n = 7), squamous cell carcinoma (n = 2), and carcinoid (n = 1). No cases of small-cell lung carcinoma or "pure lepidic" adenocarcinoma were observed.

Comment

Despite the very significant findings of the NSLT trial, lung cancer screening is still undergoing considerable discussion. This is related in part to concerns that in populations of heavy smokers, especially those with a high incidence of granulomatous disease, the large number of benign nodules that might be found could lead to unnecessary diagnostic testing and surgical intervention [17, 20].

This report describes the baseline findings of the first Brazilian lung cancer screening with LDCT (BRELT1). The screening protocol used in this program is based on international studies, particularly the NLST [7] and the International Early Cancer Action Program (I-ELCAP) [21].

The population studied in the NLST was recruited in North America where the prevalence of granulomatous disease is lower than that in Brazil. However, despite a higher positive screen rate, the application of the current guidelines for managing screen-detected nodules led to a similar incidence of patients diagnosed with lung cancer. The vast majority of lung nodules in our population had a low suspicion for cancer, even those greater than 4 or 6 mm.
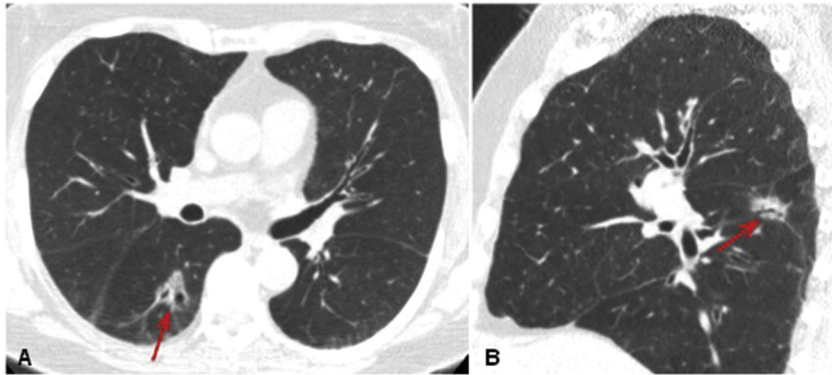
Fig 2. (A) Low-dose computed tomography (LDCT) section demonstrating 21-mm partially solid nodule in right lower lobe, which showed few dilated airways within it, so-called bubble-like lucencies (arrow). (B) Sagittal reformation better illustrates dilated airways within lesion (arrow). Follow-up resection documented an adenocarcinoma.

In the prevalence round, our results showed positive screens in 39.5% of the participants (with a 4-mm size cutoff). Also, most patients had multiple lung nodules. This value was significantly higher than in the NLST and the estimated value of other international studies. The overall results of other available studies of lung cancer screening with LDCT are summarized in Table 3.

In this study, the PPV was a little lower than in the NLST, regardless of the great difference between the numbers of patients with positive nodules. This is related to the fact that disease prevalence affects the PPV, and our lung cancer prevalence was similar to that in the NLST.

Despite a higher number of positive findings, the number of invasive procedures required was also similar to the majority of other studies, validating current workup guidelines in our population. For instance, in 42 participants with nodules larger than 8 mm,

radiologic characteristics suggested benign lesions, and only LDCT follow-up was indicated. Of note, all these patients remained stable at the 6-month follow-up examinations. Also, PET/CT helped decision making and avoided invasive procedures in 13 of 19 participants tested.

The great majority of lung cancer cases detected in this screening program were potentially curable stage IA or stage IB NSCLC (80%). This staging distribution is also similar to that seen in most of the cases detected in screening programs around the world.

As a consequence, VATS lobectomies were performed in these patients with diagnosed lung cancer. Because most screening-detected nodules are small, minimally invasive operations using video-assisted techniques (VATS or robotic operations) are optimal. The use of thoracotomy should be minimized because it may be associated with greater morbidity, especially in patients without a tissue diagnosis. Transthoracic needle biopsy was applied in 7 of 8 cases before major lung resection for malignancies. Using this approach, only 2 patients with peripheral lesions underwent diagnostic wedge resections, and the others had definitive resection by transthoracic needle biopsy. In the present study, only 1 patient was diagnosed with advanced disease (stage IIIA), and thoracotomy was indicated after neoadjuvant chemotherapy.

Furthermore, in this study, the lung cancer histologic distribution was consistent with other published screening studies. This supports the application of NLST/I-ELCAP criteria to our population. Although a high prevalence of granulomatous disease may be related to the finding of about 4,000 nodules in 790 individuals, only 25 patients ultimately met the criteria for biopsy.

Our definition of a false-positive screen makes the assumption that nodules for which we did not intervene were truly negative. This assumption was necessary to compare our results from the prevalence round. We recognize the limitation of such a calculation, because a long-term follow-up should be accomplished to confirm our findings. In this study, the false-negative rate was not calculated; this will be determined in the future by the growth of small (< 4 mm) nodules or indication for biopsy based on new LDCT findings during the follow-up period.

Table 3. Overview of LDCT Screening Trials

Study/Reference	Participants Examined with LDCT	Positivity Rate n (%)	Biopsies n (%)	Lung Cancer n (%)
NLST [7]	26,722	7,191 (27)	758 (2.8)	270 (1.0)
ELCAP [8]	1,000	233 (23)	28 (2.8)	27 (2.7)
PLuSS [9]	3,642	1,477 (41)	90 (2.5)	36 (1.0)
DLCST [10]	2,052	594 (29)	25 (1.2)	17 (0.8)
LUSI [11]	2,029	540 (27)	31 (1.5)	22 (1.1)
DANTE [12]	1,276	199 (15)	52 (4.1)	28 (2.2)
ITALUNG [13]	1,406	426 (30)	22 (1.6)	21 (1.5)
LSS [14]	1,586	325 (21)	57 (3.6)	30 (1.9)
DEPISCAN [15]	336	152 (45.2)	. . .	8 (2.4)
NELSON [16]	7,582	493 (6.5)	. . .	200 (2.6)
(Estimated Σ)	40,049	11,630 (29)	1,063 (2.7)	659 (1.6)
BRELT1	790	312 (39.5)	25 (3.1)	10 (1.3)

BRELT1 = First Brazilian Lung Cancer Screening Trial;   DANTE = Detection and Screening of Early Lung Cancer With Novel Imaging Technology;   DLCST = Danish Lung Cancer Screening Trial;   ELCAP = Early Lung Cancer Action Program;   LDCT = low-dose computed tomography;   LSS = Lung Screening Study;   LUSI = Lung Cancer Screening Intervention;   NELSON = Dutch-Belgian Randomized Lung Cancer Screening Trial (Dutch acronym);   NLST = National Lung Cancer Screening Trial;   PLuSS = Pittsburgh Lung Screening Study.

A small portion of participants (8.6%) declined further participation in the study after their initial interview. This rate is close to the rates observed in the active arm of other studies, such as ITALUNG (12.8%) [13] or DEPIS-CAN (12.7%) [15]. Even though participants voluntarily adhered to this screening program, dropouts were expected, especially because in some cases the candidates were brought to the program by their family and were not aware of the characteristics of the study.

Other limitations of this study include limited availability of occupational and environmental exposure data and the demographic characteristics and size of the sample, which may limit the ability to apply these results to the general Brazilian population because of the cultural and epidemiologic differences between the country's regions.

In summary, the results of the baseline round of the Brazilian screening program showed that the prevalence of positive LDCT scans in Brazil was much higher than in other studies, including the NLST. However, current guidelines for managing nodules are still applicable and led to a similar prevalence of NSCLC (1.3%). Also, only 3.1% of the patients required an invasive biopsy, again similar to other studies. This suggests that the prevalence of granulomatous disease did not elevate the number of false-positive results with a high suspicion for lung cancer, avoiding unnecessary biopsy/operations. A multidisciplinary team that includes thoracic surgeons, pulmonologists, and radiologists is extremely helpful in achieving these results.

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DISCUSSION

DR DANIEL L. MILLER (Marietta, GA): Dr Santos, that was an excellent presentation, and I'm glad you are bringing this to the front. We had presented our data at the Southern Thoracic in November, and being in Georgia, we have a very high incidence of histoplasmosis and sarcoidosis, and our biopsy rate was exactly the same as yours at 3%, and our benign rate was 9%. And I think as more institutions get into the screening, as you know, the CMS is supposed to approve screening if you apply for it here in March or April, so it's going to be a very detailed algorithm like you did.

What was the main driver by going on to a biopsy? Was it a change on a CT scan like an interval scan, or was it because of PET positivity? What was the reason that you went on to the next step?

DR SANTOS: That's an excellent question, Dan.

Actually, the main driver was the morphology of the nodules. We didn't have so much time to present it, but PET/CT was done in almost half of the nodules greater than 1 cm. We had 45 patients with nodules greater than 1 cm.

Also a very experienced radiologist is very important. Most of the biopsy cases had a semisolid appearance, so the morphology of semisolid plus spiculation was the main driver.

Remember this is the baseline screening that we are presenting; so far in the baseline with 1 year of follow-up, we don't have too many cases that have growth. Only 1 case was biopsied in follow-up because of small growth, so the biopsy was indicated based on the morphology and size basically.

DR MILLER: I applaud you for that because of just on 1 scan, because most people the biopsy rate would be up in the double digits, but that's excellent.

DR SCOTT J. SWANSON (Boston, MA): I enjoyed your talk. Along the lines of what you just said, what's the median follow-up of this group, and are you pretty sure you're not missing any cancers? I mean, it's a little bit of a self-fulfilling argument at this point.

DR SANTOS: Yes, that's a good point. Our intention here is to present the baseline screening, but we took care to close the accrual in July of 2014; therefore, all the patients have had at least 6 months of follow-up at this point.

We originally considered the 4-mm cutoff. More recently we have changed this for the 6 mm cutoff. We are pretty sure that all of these cases that had a positive CAT scan are followed for at least 6 months by now, but we are planning to follow everybody for at least 2 years.

We are not sure, Scott, for how long those cases with lesions that are greater than 8 mm, and have a negative PET-CT, for how long they should be followed. This is a question that we're still concerned about.

DR RICHARD K. FREEMAN (Indianapolis, IN): Again, a great paper. We are in a histoplasmosis endemic area and deal with this. Obviously serology is not helpful for that, but do you have any experience with serology or skin testing in your area for things that are endemic? Did that help you at all?

DR SANTOS: Well, this is a very interesting question. We viewed most of the guidelines for tuberculosis.. Also, Brazil is 1 of the 22 countries that are responsible for 80% of the cases of tuberculosis in the world, so I took care to review these guidelines. It's a very difficult question because in the guidelines, they mandate those serologies and the sputum tests for patients with respiratory symptoms or if they are vulnerable, with HIV for instance.

However, this study is an accrual of patients that are, quote, "asymptomatic." How do we deal with that then? Especially since a CAT scan is not a test used for screening tuberculosis.

Who the patients are that need better investigation for inflammatory disease is not that clear and was not our primary end point in this study. We found 3 cases, but certainly we could improve this pick-up rate if we appropriately investigated cases with any clinical symptoms. If you don't have significant symptoms, there is no indication to be looking for or doing extra invasive tests in these folks.

DR MATTHEW G. BLUM (Colorado Springs, CO): CMS has put together rules that suggest that we're going to need to document a preoperative consult or prescreening consultation visit, and I was curious about the mechanism of your screening program. It looked like you had a bunch of people in a room. Was that an informational meeting that talked about false-positives and radiation dosing, etc? It would be nice to have something like that that we could use to check that box for CMS.

DR SANTOS: This is a very good point. Actually, in the beginning of the program, we had a lot of problems in inviting people to participate. Prevention, as mentioned in my presentation, is not a strong point in my country, so we need to promote a lot of public information, communication through journals, TV, etc. If the national TV was involved, then we could have more people come, but 1 thing that I did personally, when the patients with negative scans came to get their results, was I went there by myself, put everybody in the same room as you saw in that image, and I explained every single detail. What is a nodule? What is the expectancy of emphysema index? What is the calcium score, the modified calcium score that we have calculated for each CAT scan? And the information on false-positives, especially after the new Canadian classification that was the lung RADS, I think it will be easier to communicate to the patients once you explain the system is that you have lung RADS-I, lung RADS-II, III, or IV and have the information better understood by this population.

I don't know if I answered your question properly.

DR BLUM: So that meeting with a room full of patients was after the scan. You got everybody together before you gave them their results?

DR SANTOS: Exactly.

DR BLUM: So it wasn't a prescan educational piece?

DR SANTOS: Yes, actually we had both, an explanation before scan for the informed consent signature, and after the scan I got everybody together with negative results. If they had positive results, then it would be a one-to-one conversation in the medical clinic consultation with the pulmonologist or the thoracic surgeon.

Also for all the positive results we had a biweekly meeting where we had the whole multidisciplinary group discussing to make sure the approach that we give to the patient would be consistent.

DR FRANK C. DETTERBECK (New Haven, CT): Just a comment about the increase to 6 mm to make sure that we're all thinking about things carefully. If you only look at 1 thing like what is the incidence of positive scans, sure, bump it up to 6 mm, your number goes down. It looks good. Bump it up to 10 mm, looks better, and so forth, but all of this is a complex interplay, and as you bump that number up, your ability to detect cancers that are very early becomes a little bit less. Your compliance rate, whether people come back for a follow-up scan, becomes much more important, and if your compliance rate starts to be a little bit less, then it could be that we end up not making much progress. So we just have to be careful that we think about all these things carefully and we don't look at just 1 number and think that we've got the answer without really understanding what the effects are on all of the other aspects.

DR SANTOS: Thank you, Frank, for your comment. I agree with you, but there's 1 thing that's very important for the population study, which are the costs, and when you see that we had 166 CAT scans done for patients with 4- to 6-mm nodules and only 1 patient got a biopsy. Actually, this was a negative one because this patient had a 0.5-cm endobronchial lesion that we ruled to be an hamartoma, this is the only case that we did a biopsy in 4 to 6 mm.

So, I believe it needs to be a balance between costs and proper information for the patient. Actually, 9.6% of the patients that came to get a CAT scan, a free CAT scan in a private hospital, didn't actually come back to do the test, so 1 in 10 patients failed to return for the first test.

So this is really important what you're saying, and this is a cultural thing that we need to improve. We need good communication to make sure that patients with positive or negative results will come back 1 year afterward, so we're talking about the adherence of the CT screening baseline and follow-up, and I totally agree with you.

Just to finish, we are following closer the 6-mm cutoff, but again, greater than 4 mm we are getting registered. We put in the paper all the nodules listed. We are not leaving without seeing those nodules. It's just not to be considered as positive. Thank you very much.