Cone-beam CT and Augmented Fluoroscopy–guided Navigation Bronchoscopy

Radiation Exposure and Diagnostic Accuracy Learning Curves

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Background: The endobronchial diagnosis of peripheral lung lesions suspected of lung cancer remains a challenge from a navigation as well as an adequate tissue sampling perspective. Cone-beam computed tomography (CBCT)
guidance is a relatively new technology and allows for 3-dimensional imaging confirmation as well as navigation and biopsy guidance, but, also involves radiation. This study investigates how radiation exposure and diagnostic accuracy in the CBCT-guided navigation bronchoscopy evolves with increasing experience, and, with a specific tailoring of CBCT and fluoroscopic imaging protocols towards the procedure.

Patients and Methods: In this observational clinical trial, all 238 consecutive patients undergoing a CBCT-guided navigation bronchoscopy from the start of our CBCT-guided navigation bronchoscopy program (December 2017) until June 2020 were included. Procedural dose characteristics and diagnostic accuracy are reported as a function of time.

Results: Procedural radiation exposure as measured by the dose area product initially was 47.5 Gy·cm² (effective dose: 14.3 mSv) and gradually reduced to 25.4 Gy·cm² (5.8 mSv). The reduction in fluoroscopic dose area product was highest, from 19.0 Gy·cm² (5.2 mSv) to 2.2 Gy·cm² (0.37 mSv, 88% reduction), despite a significant increase of fluoroscopy time. The diagnostic accuracy of navigation bronchoscopy increased from 72% to 90%.

Conclusion: A significant learning effect can be seen in the radiation safety and diagnostic accuracy of a CBCT-guided and augmented fluoroscopy-guided navigation bronchoscopy. With increasing experience and tailoring of imaging protocols to the procedure, the procedural accuracy improved, while the effective dose for patients and staff was reduced.

Key Words: cone-beam computed tomography, navigation bronchoscopy, peripheral pulmonary lesions radiation safety, early-stage lung cancer

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Peripheral lung lesions with intermediate to high risk of malignancy should preferably be diagnosed by minimally invasive means before deciding upon a treatment strategy.1–4 The currently available most sensitive options for obtaining samples
from peripheral lung lesions include computed tomography (CT)-guided transthoracic needle biopsy and technology-enhanced endobronchial approaches. CT-guided transthoracic needle biopsy has an overall sensitivity of ~90%3,5 but is also associated with a 19% to 25% risk of pneumothorax.5 The endobronchial approach as enhanced by different means of technology has shown a 70% to 77% pooled sensitivity in the meta-analysis, with only a 1.5% to 2.0% risk of pneumothorax.6,7 Recently, it was shown that utilizing intraprocedural cone-beam computed tomography (CBCT) image guidance—a relatively new technique in this field—may retain complication risk while further increasing the accuracy of this technology-enhanced navigation bronchoscopy procedure.8,9 Aside of its unique ability to acquire intraprocedural 3-dimensional (D) information, deemed valuable for meticulous positioning of tools, the CBCT system can also augment a navigation pathway and lesion position as an overlay on 2D fluoroscopic imaging (also termed augmented fluoroscopy, AF). With this combination of features, CBCT has the potential to meticulously help guide the endoscopist during the different aspects of the procedure.

The use of CBCT imaging systems for guiding the endobronchial diagnosis of suspected peripheral pulmonary lesions solely relies on x-ray imaging through both AF imaging as well as repeated CBCT’s to navigate and confirm positioning. Since only a few reports describe CBCT and AF use in interventional pulmonology, little is known about its radiation safety profile. Steinfort et al10 and Casal et al11 report effective CBCT-guided bronchoscopy procedural dose ranges of 9 to 60.8 and 11 to 29 mSv (dose area product, DAP: 64.6 Gy·cm²), whereas Pritchett et al12 report a procedural DAP of only 31 Gy·cm² and an effective procedural dose estimation as low as 3 mSv.

We hypothesize the radiation exposure to both patients and staff might vary significantly, as it is subject to a learning curve experience. Therein, not only the endoscopist is likely to change its radiation use as experience increases. Tailoring of the CBCT system to the requirements of this relatively new field is also of likely effect. Changing system imaging quality and collimation options could enhance radiation safety to that purpose, without negatively affecting diagnostic accuracy.

In this study, we prospectively evaluate unselected consecutive navigation bronchoscopy cases to study 2 (possibly interrelated) topics: (1) the radiation exposure in the primarily CBCT-guided navigation bronchoscopy procedure over time (with the tailoring of imaging protocols specific to the procedure); (2) the procedural diagnostic accuracy in the CBCT-guided and AF-guided navigation bronchoscopy over time. We hypothesize that more procedural experience and specific tailoring of CBCT and AF imaging protocols to the navigation bronchoscopy procedure may significantly reduce radiation dose while maintaining or improving procedural accuracy.

**PATIENTS AND METHODS**

**Patient Inclusion**

This prospective single-center study was approved by the local ethical committee. All consecutive patients in the period December 2017 to June 2020 without contraindications for an endobronchial procedure and a peripheral pulmonary lesion for whom a minimally invasive biopsy was indicated and performed according to routine clinical care were eligible for study inclusion. In our center, CBCT and AF guidance was the first choice of procedure (preferred over transthoracic needle aspiration) but only indicated for those lesions where advanced navigation guidance and confirmation was deemed necessary (location at least beyond second-order branches of segmental bronchi). In cases where lesions were thought to be reachable by catheters under radial endobronchial ultrasound (r-EBUS) miniprobe imaging (UM-S20-17S; Olympus, Tokyo, Japan) and C-arm fluoroscopy guidance, procedures were not performed on the CBCT imaging suite. Written informed consent was obtained in all cases. Patients eventually reached and diagnosed without CBCT imaging were excluded from this study. All procedures were performed by the same team of 1 interventional pulmonologist and 1 technical physician.

**Methods**

Procedures were performed under general anesthesia. Standard flexible video bronchoscopes with a 2.8 mm working channel (EB19-J10; Pentax Medical, Tokyo, Japan) were used for inspection bronchoscopy and subsequent navigation guidance of commercially available catheters. Catheter navigation was performed only on basis of CBCT and AF guidance in all but the cases where electromagnetic navigation technology
(EMN; Medtronic SuperDimension, Minneapolis, MN) was additionally used (Fig. 1). After navigation, r-EBUS miniprobes and/or CBCT with AF imaging were routinely used to confirm lesion access. Consecutive tissue sampling was performed under the guidance of AF. The tissue sampling methodologies used and the number of samples taken were decided upon by clinical decision-making and routinely included a selection of 1 or more tools in the following order: brushing, transbronchial needle aspiration, biopsy forceps, cryobiopsy, lavage. The sampling method with every tool remained constant throughout the study. Rapid on-site evaluation of cytopathology was always available.

The navigation bronchoscopy procedures were performed on 3 CBCT systems; a ceiling-mounted Philips Allura Clarity FD20 scanner which was later replaced by a ceiling-mounted Philips Azurion scanner (Philips, Best, The Netherlands), and, a floor-mounted Siemens Artis Zeego scanner (Siemens Healthineers, Forchheim, Germany). As part of specific research collaboration, dedicated imaging protocols and software were installed and updated only on the Philips systems. Distinct periods and concurrent imaging methods on these imaging systems can be defined (Fig. 1). To allow for an accurate learning experience description, the radiation exposure is reported only for the Philips imaging systems. In enabling a description of the diagnostic accuracy learning curve experience, the procedures on all platforms are however taken into account.

X-ray Imaging

In short, our navigation bronchoscopy program started with imaging protocols only focusing on acquiring the highest imaging quality possible. However, navigation bronchoscopy is not all about maximum image quality and should adhere to the ALARA principle (As Low As

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**FIGURE 1.** Flow chart of study inclusion. AF indicates augmented fluoroscopy; CBCT, cone-beam computed tomography; CT, computed tomography; EMN, electromagnetic navigation; NSCLC, non–small cell lung cancer.
Reasonably Achievable). As tools and lesions can often be distinguished from the surrounding lung tissue in navigation bronchoscopy after having obtained initial guidance information, not every detail on subsequent CBCT scans or fluoroscopy imaging is needed. We, therefore, changed the availability of thorax CBCT scanning and AF protocols from 1 to 3 options. Therewith, quality and concurrent radiation dose could be dynamically decided upon by the endoscopist. For instance, the necessary image quality could be based on requiring only relative positioning information (low dose), identifying if a ground glass lesion had been accurately accessed (medium dose) or to identify different bronchi for navigation towards the lesion (high/ original dose, Fig. 2). The goal of these dedicated imaging protocols was to provide multiple options to the endoscopist, retaining diagnostic accuracy while maintaining or decreasing radiation dose. Protocol changes were made in due time (Fig. 1). First low-dose fluoroscopy protocols became available, afterwards, low-dose CBCT protocols. When the Philips Allura system was replaced by the Azurion system, low-dose fluoroscopy protocols were immediately transferred. Ten procedures however passed before the low-dose CBCT protocols were made available on the Azurion system.

Analysis

Primary study parameters are radiation dose and diagnostic accuracy (over time) in a primary CBCT and AF approach, linked to an initial—generic—imaging protocol and the forthcoming availability of dedicated navigation bronchoscopy imaging protocols (over time).

Radiation Exposure

To evaluate radiation exposure of navigation bronchoscopies primarily guided by CBCT and AF, cases where other technological modalities were used as primary guidance were excluded for radiation exposure analysis (Fig. 1). Radiation dose information was obtained using openREM software. The procedural dose was routinely reported through the DAP. The retrospectively computed effective dose (in mSv) is a less reliable dose estimate because its computation requires several parameters that are difficult to estimate in a continuously changing setting such as with CBCT and AF. For enabling comparison against other imaging modalities, a limited set of average effective doses were, however, calculated with PCXMC. For quantitative analysis of radiation dose (over time), boxplots and Shewhart individual control charts of accumulated DAP and counts are presented, further tested for significant differences by Kruskal-Wallis and analysis of variance tests.

Diagnostic Accuracy

To evaluate the continuous diagnostic accuracy of a catheter-based navigation bronchoscopy as primarily or secondarily guided by

FIGURE 2. Example images subsequently obtained from low-dose (A) and normal-dose (B) imaging protocols for navigating towards a 6x8 mm lesion found in the apical segment of the left lower lobe. As can be seen, artifacts alike the classically known streaking can be seen more strongly in the low-dose protocol. Although difficult to appreciate on still images, there is also a further difference in image quality for, that is, allowing recognition of the smallest of bronchi that can be navigated to. Note the minor bleeding lateroposterior to the lesion on the image (B) after having performed an initial biopsy.
CBCT and AF in this single-institution setting, all navigation bronchoscopies were included (Fig. 1). Navigation success is defined as cases where imaging gives no doubt about lesion access as confirmed by at least CBCT with AF imaging, but can also include unambiguous r-EBUS imaging or ROSE outcome. Malignant and specific benign findings are considered true positive and negative if not negated by follow-up findings, respectively. Unspecific benign findings are considered true negative only if definitively confirmed by follow-up CT-guided transthoracic needle aspiration, surgical biopsy, and/or decisive clinical follow-up of at least 6 months (ie, no measurable growth). Unrepresentative findings or unsuccessful navigations are considered false negatives regardless of follow-up outcome. The diagnostic accuracy is obtained by relating summed number of true positives and true negatives to the total number of procedures. Time-dependent parameters are described by moving averages (10 procedures).

Dichotomous variables were analyzed by the Pearson \( \chi^2 \) test or Fisher exact test. Not normally distributed continuous variables were evaluated by the Mann-Whitney-Wilcoxon test. Procedural trends over time were evaluated by the Spearman test. All P-values were 2 sided and considered significant if <0.05. R and R-studio were used for statistical analysis.16

RESULTS

Patients with informed consent were included from the initiation of our CBCT-guided and AF-guided navigation bronchoscopy program (December 2017) until June 2020 (n = 238, Fig. 1). Exclusion of patients was performed for radiation dose evaluation in cases of a missing radiation report (10), a nonprimary CBCT and AF-based navigation (58), and, cases where navigation bronchoscopy was not performed on the systems under study (40), leaving 100 cases for analysis. Second, 208 patients were eligible and prospectively included for the diagnostic accuracy analysis in this study. These 208 patients had a total of 248 lesions that were navigated to, with a median long-axis diameter of 13 mm (range: 5 to 65 mm, Table 1).

Radiation Exposure

At the start of our CBCT-guided and AF-guided navigation bronchoscopy program, the average procedural DAP was 47.5 Gy·cm²

| TABLE 1. Patient, Nodule, and Procedural Characteristics |
|---------------------------------------------------------|
| Patient characteristics                                 |
| Patients/lesions (n) 208/248                             |
| Sex: male/female [n (%)] 114 (55)/94 (45)                |
| Age (y), length (m), weight (kg), BMI (kg/m²) [mean (minimum-maximum)] 65 (36-85), 1.72, 74.9, 25.3 |

Nodule and procedural characteristics

| Lesion diameter [median (minimum-maximum)] (mm) 13 (5-65) |
|---------------------------------------------------------|
| Bronchus sign (at ≤ 1 mm CT, lesions) (%) 60.9 |
| Navigation time [median (minimum-maximum)] (min) 29 (4-100) |
| Biopsy time [mean (SD)] (min) 25.6 (10.74) |
| Tissue samples taken [mean (minimum-maximum)] 11 (0-25) |

Lesion locations n

| LUL/RUL 67/85 |
| --------------|
| —/RML —/11 |
| LLL/RLL 37/48 |

Procedural outcome

| Lesion long-axis size (mm) |
|---------------------------|
| N | Navigation success [n (%)] | Diagnostic accuracy (patients) [n (%)] | Malignancy prevalence (%) |
|---------------------------|
| ≤ 10 | 36 | 33 (91.6) | 25 (69.4) | 75 |
| > 10-20 | 113 | 100 (88.5) | 83 (73.5) | 71.2 |
| > 20-30 | 32 | 32 (100) | 27 (84.4) | 80.6 |
| > 30 | 27 | 27 (100) | 24 (88.9) | 74.1 |
| Overall 208 | 92.3% | 76.4% | 73.7 |

Bronchus sign—Image feature showing the lesion to be directly adjacent to a bronchus. Navigation success—CBCT imaging and/or unambiguous radial endobronchial ultrasound imaging verified access of the lesion. Diagnostic accuracy (pat)—Procedural outcome of navigation bronchoscopy corresponding to follow-up outcome (see the Patients and methods section).

BMI indicates body mass index; CBCT, cone-beam computed tomography; CT, computed tomography; LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.
(effective dose: 14.3 mSv). The initial average fluoroscopic DAP was 19.0 Gy·cm\(^2\) (5.2 mSv) and the initial total CBCT scan DAP as a consequence of performing 2.47 rotations per procedure was 29.9 Gy·cm\(^2\) (9.1 mSv, 3.7 mSv/scan). As experience increased and the different fluoroscopic and CBCT imaging protocols gradually became available (along with the replacement of the CBCT system, Fig. 1), procedural DAP gradually declined from 47.5 (estimated effective dose: 14.3 mSv, initial period with original protocols) to 25.4 Gy·cm\(^2\) (5.8 mSv, low-dose CBCT and fluoroscopy protocols on new Azurion CBCT system). Boxplots and Shewhart individual control charts of DAP per period can be found in Figure 2 and Supplemental Figure 1 (Supplemental Digital Content 1, http://links.lww.com/LBR/A225), respectively. Table 2 summarizes the average radiation characteristics per period.

The most important cause of the reduction in procedural radiation exposure was an altered use of fluoroscopy (Fig. 3, Supplemental Fig. 1B, Supplemental Digital Content 1, http://links.lww.com/LBR/A225). Becoming more experienced and implementing lower dose fluoroscopy protocols changed average fluoroscopy DAP from 19.0 Gy·cm\(^2\) (effective dose: 5.2 mSv) to 2.2 Gy·cm\(^2\) (0.37 mSv, \(P < 0.01\)). This is counterintuitive to what one would expect based on the monitoring of average total procedural fluoroscopy time. The initial average total fluoroscopy time was 592 seconds (9.9 min), and it gradually increased to an average of 935 seconds (15.6 min, \(P < 0.01\), Fig. 3, Supplemental Fig. 1E, Supplemental Digital Content 1, http://links.lww.com/LBR/A225).

In the last study period, the bulk of radiation exposure was caused by CBCT acquisitions. While the individual average CBCT scan exposure changed significantly when comparing first to last scanning period (from 12.1 to 8.8 Gy·cm\(^2\), \(P < 0.01\), Fig. 3, Supplemental Fig. 1D, Supplemental Digital Content 1, http://links.lww.com/LBR/A225), total CBCT scan exposure did not (from an average of 29.9 to 23.4 Gy·cm\(^2\), \(P = 0.24\), Fig. 3, Supplemental Fig. 1C, Supplemental Digital Content 1, http://links.lww.com/LBR/A225). This can be attributed to an increase in the average number of CBCTs performed per procedure, from 2.47 to 2.93 (nonsignificant, Fig. 3, Supplemental Fig. 1F, Supplemental Digital Content 1, http://links.lww.com/LBR/A225).

### Diagnostic Accuracy

A primary CBCT and AF approach was performed in 150/208 cases. A primary EMN approach was performed in the remaining 58 cases, with 40 of these cases taking place in the first 87 patients during the conduct of our previous study (comparing the EMN and CBCT approach).\(^9\) The diagnostic accuracy when taking into account all 208 consecutive procedures was 76.4% (Table 1). After concluding our previous trial comparing the EMN and CBCT approach at the beginning of 2019 (87 patients, diagnostic accuracy: 72.4%\(^9\)), a temporary drop in accuracy is seen. This drop cannot be explained solely by factors like bronchus sign, lesion size,

### Table 2. Average Radiation Dose Characteristics Per Period, as Defined Per Imaging Protocols Available (Fig. 1)

| Time Period (n) | System | Fluoroscopy Protocol | DAP (Gy·cm\(^2\)) | Time (s) | CBCT Protocol | DAP/Acq. Acq. | Total DAP |
|-----------------|--------|----------------------|-------------------|---------|---------------|---------------|-----------|
| Period 1 (n=26) | Allura | Original dose        | 19.0              | 592     | Original dose | 12.1          | 47.5      |
| Period 2 (n=7)  | Allura | Low dose             | 7.1               | 817     | Low dose      | 13.6          | 45.3      |
| Period 3 (n=24) | Azurion| Low dose             | 2.2               | 935     | Original dose | 13.8          | 28.2      |
| Period 4 (n=13) | Azurion| Low dose             | 8.8               | 2.93    |               |               | 25.4      |

At first instance, the Allura CBCT imaging system was available with original dose imaging protocols for both fluoroscopy and CBCT (n = 26). From there on, consecutive changes were made in the system, fluoroscopy, or CBCT availability.

DAPs are given for every subsequent period in Gy·cm\(^2\).

Also see corresponding Figure 1 and Supplemental Figure 1 (Supplemental Digital Content 1, http://links.lww.com/LBR/A225).

Acq. indicates CBCT rotational acquisition; CBCT, cone-beam computed tomography; DAP, dose area product.
**FIGURE 3.** Boxplots of radiation dose over time and per protocol becoming available (left to right). Box indicates first to the third quartile, a line indicating median. A, Total procedure radiation DAP. B, Procedural fluoroscopy DAP. C, Procedural CBCT DAP. D, Individual CBCT DAP. E, Procedural fluoroscopy time (s). F, Amount of CBCT performed per procedure. Also see Figure 1, for period partitioning based on CBCT system and protocol availability and Supplemental Figure 1 (Supplemental Digital Content 1, http://links.lww.com/LBR/A225) for corresponding Shewhart individual control charts of radiation exposure data. CBCT indicates cone-beam computed tomography; DAP, dose area product.
malignancy prevalence, or a decline in navigation success (all \( P > 0.05 \)). In the subsequent period, dynamical decision-making by the endoscopy team led to increasing the number of biopsy samples obtained, as CBCT remained to consistently show accurate lesion access (Fig. 4). Over the next period, diagnostic accuracy gradually rose. From November 2019 to June 2020, the overall diagnostic accuracy was 90.6%, whereas navigation success was 98.4% (n = 64 procedures).

Statistical analysis of overall procedural characteristics revealed that lesion size did not change significantly over time (Spearman \( \rho: -0.02, P = 0.74 \)). However, a bronchus sign was present significantly less often over time (Spearman \( \rho: -0.26, P < 0.01 \)). The malignancy prevalence, bronchus sign presence, and transparenchymal navigation did not have a significant effect on overall diagnostic accuracy. Variables that were statistically related to higher diagnostic accuracy were higher lesion diameter (\( P = 0.014, 9 \) vs. 15 mm median size), navigation success (\( P < 0.001 \)), and a higher number of tissue samples having been obtained (\( P < 0.001, \) median 10 vs. 12 samples).

**The Learning Curve Effect**

The learning effect can be derived from combining the information from both radiation exposure as well as diagnostic accuracy in navigation bronchoscopy guided by CBCT and AF are subject to a significant learning effect. An increase in experience and tailoring of imaging protocols towards the procedure significantly reduced the radiation exposure while the diagnostic accuracy was enhanced. Total procedural DAP went down from 47.5 Gy·cm\(^2\) (effective dose: 14.3 mSv) to 25.4 Gy·cm\(^2\) (5.8 mSv), while the diagnostic accuracy went up from 72% to 90%. The learning effect in radiation safety is greatest in the use of fluoroscopy, where the total use time went up significantly (\( P < 0.01 \)), while a significant reduction in its exposure could simultaneously be seen (\( P < 0.01 \), Fig. 3, Supplemental Figs. 1B, E, Supplemental Digital Content 1, http://links.lww.com/LBR/A225).

**DISCUSSION**

We show in a prolonged case series that radiation exposure as well as diagnostic accuracy in navigation bronchoscopy guided by CBCT and AF are subject to a significant learning effect. An increase in experience and tailoring of imaging protocols towards the procedure significantly reduced the radiation exposure while the diagnostic accuracy was enhanced. Total procedural DAP went down from 47.5 Gy·cm\(^2\) (effective dose: 14.3 mSv) to 25.4 Gy·cm\(^2\) (5.8 mSv), while the diagnostic accuracy went up from 72% to 90%.

The ALARA principle dictates to use radiation as sparsely as possible. The recent forthcoming availability of specific imaging protocols for navigation bronchoscopy that facilitate different steps of the procedure with specific imaging quality shows to help the goal of reducing the dose. Interestingly, the significant reduction in radiation dose as seen in our study persisted even though the 2D fluoroscopy time and number of CBCTs performed per procedure increased over time (Fig. 3, Supplemental Fig. 1, Supplemental
Digital Content 1, http://links.lww.com/LBR/A225). Arguably, the increase in use may be caused by awareness in the reduction of radiation dose by newer protocols. We feel having additional imaging options with a lower dose lowered the threshold for additional (confirmatory) imaging. In turn, this additional confirmation might have increased our diagnostic accuracy by more meticulous positioning.

In an increasingly crowded technology field for aiding the diagnosis of peripheral pulmonary lesions, the endoscopist likely has to choose between different technological guidance modalities or which combination to use. The endoscopist should aim for high accuracy, keep the amount of radiation involved as low as possible, and, simultaneously, take into account the procedural costs. We previously showed that using CBCT and AF only after having performed EMN significantly reduced fluoroscopy time and the amount of CBCT scans performed. In the current study, we show the radiation dose has decreased significantly since. And while the patient will receive both CBCT as well as fluoroscopy dose, the staff dose is mainly caused by fluoroscopic exposure (as they leave the area during CBCT). Considering the accuracy of the CBCT-guided navigation bronchoscopy, the procedural radiation burden for the patient when related to other procedures, and the associated cost of some of the additional navigation guidance modalities, one needs to individually assess if having multiple navigation guidance modalities remains worthwhile. On the basis of our experience, the added value of CBCT and AF when compared with other non–real-time navigation technology such as EMN is greatest in lesions needing more meticulous positioning. Meticulous positioning is, for example, especially relevant in cases with: no bronchus sign (small lesions and/or metastatic disease), pleural positioning, or, navigations of the more easily deformable lower lobes where multiple bronchi are often parallel and subject to considerable breathing motion. Additional studies evaluating the correlation between specific procedural and lesion characteristics in an experienced user setting are necessary to evaluate how and which procedural characteristics affect the procedural accuracy and radiation dose.

As CBCT and AF guidance allows for biopsy with great detail, an elaborate reflection on technique is possible. Shortly after completing our previous study, we observed a decline in diagnostic accuracy (Fig. 4). As we have real-time CBCT imaging information available and discuss all cases in the multidisciplinary tumor board shortly following the procedure, we concluded that inadequate tissue acquisition after successful navigation was a likely cause of error. Following these findings, more time was spent on tissue acquisition. Consecutively, the diagnostic accuracy improved to as much as 90.6% in the last 64 procedures (November 2019 to June 2020). We experience that having confirmed biopsy positioning on CBCT also provides additional certainty in case of benign pathology findings.

**Study Limitations**

The reduction in radiation dose—as time passed and the team became more experienced—was caused by both dedicated protocols as well as more aggressive collimation and targeted imaging. Detailed collimation information was not available in our dataset and could therefore not be presented. Furthermore, it is difficult to evaluate how our single-center results equate to other centers. For one, average patient body mass index should be taken into account (25 in this study, Table 1), as this might significantly affect radiation use outcomes. Another limitation herein was our continuous awareness of radiation safety, as it was directly under study. This might have significantly attributed to an increased learning speed.

Our report was based on a prospective collection of consecutive cases. There was no preselection of patients other than an indication for tissue sampling. We did not observe any changes in patient or nodule characteristics in the time frame of this study that could explain the improved accuracy or reduced radiation exposure over time. Analysis of known factors influencing yield such as lesion size and bronchus sign presence did not logically correlate to our improved accuracy and dose parameter findings. The bronchus sign presence decreased significantly over time while lesion size did not significantly change. However, we cannot fully exclude the possibility that some variation in outcomes might be related to distinct (other) procedural parameters.

Finally, the follow-up time for nonmalignant findings in this study was limited to at least 6 months. Although we strictly defined our diagnostic criteria in order not to overestimate the diagnostic accuracy, it is possible that a longer follow-up could slightly influence our calculated accuracy.

**CONCLUSIONS**

In this single-institution study, we show radiation dose of a CBCT-guided and AF-guided
Navigation bronchoscopy are of acceptable levels but also subject to a significant learning effect. With the implementation of new specified navigation bronchoscopy imaging protocols along with increasing experience, procedural radiation dose could be reduced from 47.5 Gy·cm² (effective dose: 14.3 mSv) to 25.4 Gy·cm² (5.8 mSv), while the diagnostic accuracy increased from 72% to 90%. Navigation bronchoscopy using CBCT and AF imaging as a sole technique for both navigation and sampling is a (relatively) safe and accurate procedure for diagnosis of small peripheral pulmonary lesions.

REFERENCES
1. Ettinger DS, Wood DE, Aggarwal C, et al. Guidelines on non-small cell lung cancer v1. J Natl Compr Cancer Netw. 2020.
2. Gould MK, Donington J, Lynch WR, et al. Evaluation of individuals with pulmonary nodules: When is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American college of chest physicians evidence-based clinical practice guidelines. Chest. 2013;143:e93s–e120s.
3. Callister MEJ, Baldwin DR, Akram AR, et al. BTS guidelines for the investigation and management of pulmonary nodules. Thorax. 2015;70:i1–i54.
4. Louie AV, Senan S, Patel P, et al. When is a biopsy-proven diagnosis necessary before stereotactic ablative radiotherapy for lung cancer? A decision analysis. Chest. 2014;146:1021–1028.
5. Heerink WJ, Bock GH de, Jonge GJ de, et al. Complication rates of CT-guided transthoracic lung biopsy; meta-analysis. Eur Radiol. 2017;27:138–148.
6. Folch EE, Labarca G, Ospina-Delgado D, et al. Sensitivity and safety of electromagnetic navigation bronchoscopy for lung cancer diagnosis. Chest. 2020;158:1753–1769.
7. Wang Memoli JS, Nietert PJ, Silvestri GA. Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. Chest. 2012;142:385–393.
8. Pritchett MA, Schampaert S, Groot JAH De, et al. Cone-beam CT with augmented fluoroscopy combined with electromagnetic navigation bronchoscopy for biopsy of pulmonary nodules. J Bronchology Interv Pulmonol. 2018;25:274–282.
9. Verhoeven RLJ, Fütteler JJ, Hoflsaot W, et al. Cone-beam CT image guidance with and without electromagnetic navigation bronchoscopy for biopsy of peripheral pulmonary lesions. J Bronchology Interv Pulmonol. 2021;28:60–69.
10. Steinfurt DP, D’Agostino RD, Vrijlic I, et al. CT-fluoroscopic guidance for performance of targeted transbronchial cryobiopsy: a preliminary report. Respiration. 2018;96:472–479.
11. Casal RF, Sarkiss M, Jones AK, et al. Cone beam computed tomography-guided thin/ultrathin bronchoscopy for diagnosis of peripheral lung nodules: a prospective pilot study. J Thorac Dis. 2018;10:6950–6959.
12. Pritchett M, Radaelli A, Schampaer t S, et al. Cone beam CT-guided endobronchial biopsy assisted by augmented fluoroscopy. Chest. 2017;152:A887.
13. McDonagh E. OpenREM—Free and open source radiation exposure monitoring for the physicist, V.0.9.0. Available at: http://openrem.org.
14. ICRP, 2015. Radiological Protection in Cone Beam Computed Tomography (CBCT). ICRP Publication 129. Ann. ICRP 44(1). Available at: https://www.icrp.org/publication.asp?id=ICRP%20Publication%20129.
15. Tapiovaara M, Lakkisto M, Servomaa A, et al. A PC based Monte Carlo program for calculating patient doses in medical x-ray examinations; 2008.
16. R Core Team. R: a language and environment for statistical computing; 2019. Available at: www.r-project.org.