REVIEW ARTICLE

Management of Progressive Pulmonary Nodules Found during and outside of CT Lung Cancer Screening Studies

Mathias Meyer, MD,[a,*] Rozemarijn Vliegenthart, MD, PhD,[b] Thomas Henzler, MD,[a] Daniel Buergy, MD,[c] Frank A. Giordano, MD,[c] Michael Kostrzewa, MD,[a] Nils Rathmann, MD,[a] Odd Terje Brustugun, MD, PhD,[d] Lucio Crino, MD, PhD,[e] Anne-Marie C. Dingemans, MD, PhD,[f] Michael Dusmet, MD,[g] Dean Fennell, MD, PhD,[h] Dominique Grunenwald, MD, PhD,[i] Rudolf Maria Huber, MD, PhD,[j] Marcin Moniuszko, MD, PhD,[k] Francoise Mornex, MD, PhD,[l] Mauro Papotti, MD,[m] Lothar Pilz, PhD,[n] Suresh Senan, MD, PhD,[o] Kostas Syrigos, MD, PhD,[p] Maurice Pérol, MD,[q] Jhanelle E. Gray, MD,[r] Christoph Schabel, MD,[s] Jan P. van Meerbeeck, MD, PhD,[t] Nico van Zandwijk, MD, PhD,[u] Cai Cun Zhou, MD, PhD,[v] Christian Manegold, MD, PhD,[w] Wieland Voigt, MD,[x] Eric Dominic Roessner, MD[w]

[a]*Institute of Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim, Mannheim, Germany*
[b]*Center for Medical Imaging North-East Netherlands, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands*
[c]*Department of Radiation Oncology, University Medical Center Mannheim, Mannheim, Germany*
[d]*Section of Oncology, Drammen Hospital, Vestre Viken Hospital Trust, Drammen, Norway*
[e]*University Medical School of Perugia, Azienda Ospedale Perugia, Perugia, Italy*
[f]*Department of Pulmonology, GROW-School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands*
[g]*The Royal Brompton Hospital, London, United Kingdom*
[h]*University Hospitals Leicester, Leicester, United Kingdom*
[i]*Department of Thoracic Surgery, Tenon Hospital, Paris, France*
[j]*Department of Medicine, Thoracic Oncology Centre Munich Ludwig Maximilians University, Deutsches Zentrum für Lungenforschung (Comprehensive Pneumology Center Munich), Munich, Germany*
[k]*Department of Regenerative Medicine and Immune Regulation, Medical University of Bialystok, Białystok, Poland*
[l]*Department of Radiation Oncology, Centre Hospitalier Lyon Sud, Lyon, France*
[m]*Department of Oncology, University of Turin, Turin, Italy*
[n]*Department of Biostatistics, University Medical Center Mannheim, Mannheim, Germany*
[o]*Department of Radiation Oncology, VU University Medical Center Amsterdam, Amsterdam, The Netherlands*
[p]*Sotiria General Hospital, Athens School of Medicine, Athens, Greece*
[q]*Department of Medical Oncology, Léon Bérard Cancer Center, Lyon, France*
[r]*Department of Thoracic Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida*
[s]*Department for Diagnostic and Interventional Radiology, Eberhard Karls University Tübingen, University Hospital Tübingen, Tübingen, Germany*
[t]*Thoracic Oncology/Multidisciplinary Oncologic Centre, Antwerp University Hospital, University of Antwerp, Antwerp, Belgium*
[u]*Asbestos Diseases Research Institute, University of Sydney, Sydney, New South Wales, Australia*
[v]*Department of Lung Cancer and Immunology, Shanghai Pulmonary Hospital, Tongji University Medical School Cancer Institute, Tongji University School of Medicine, Wuhan, People's Republic of China*

*Corresponding author.

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Address for correspondence: Mathias Meyer, MD, Institute of Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim, Medical Faculty Mannheim-Heidelberg University, Theodor-Kutzer-Ufer 1-3, Mannheim D-68167, Germany. E-mail: mathias.meyer@medma.uni-heidelberg.de

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[w]Division of Surgical Oncology and Thoracic Surgery, Department of Surgery, University Medical Center Mannheim, Mannheim, Germany
[x]Medical Innovation and Management, Steinbeis University Berlin, Germany

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ABSTRACT

Although the effectiveness of screening for lung cancer remains controversial, it is a fact that most lung cancers are diagnosed at an advanced stage outside of lung cancer screening programs. In 2013, the U.S. Preventive Services Task Force revised its lung cancer screening recommendation, now supporting lung cancer screening by low-dose computed tomography in patients at high risk. This is also endorsed by many major medical societies and advocacy group stakeholders, albeit with different eligibility criteria. In Europe, population-based lung cancer screening has so far not been recommended or implemented, as some important issues remain unresolved. Among them is the open question of how enlarging pulmonary nodules detected in lung cancer screening should be managed. This article comprises two parts: a review of the current lung cancer screening approaches and the potential therapeutic options for enlarging pulmonary nodules, followed by a meeting report including consensus statements of an interdisciplinary expert panel that discussed the potential of the different therapeutic options.

Keywords: Pulmonary nodules; Lung cancer screening; Surgery; Stereotactic ablative radiotherapy

Introduction

As the largest lung cancer screening trial conducted so far, the National Lung Screening Trial (NLST) (in which 53,000 individuals were screened) showed a 20% reduction in lung cancer–related mortality with low-dose computed tomography (LDCT) screening in current or former heavy smokers versus with radiographic screening.[1] In Europe, the largest randomized lung cancer computed tomography (CT) screening trials include the Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON [known in English as the Dutch-Belgian Lung Cancer Screening Trial]) (16,000 screenees and controls) and the United Kingdom Lung Cancer Screening trial (4000 screenees and controls).[2,3] LDCT screening trials have shown a much higher percentage of stage I disease (50%–82%) compared with general practice outside of screening programs, in which the rate of stage I disease is usually less than 20%.[3] Several U.S. guidelines have recommended lung cancer screening in high-risk individuals, although with different eligibility criteria.[4–6] In the United States, lung cancer screening has been recommended, conducted, and reimbursed since early 2015.[7] The only European statement (European Society of Radiology/European Respiratory Society white paper on lung cancer screening) restricts screening to longitudinal, quality-assured programs within clinical trials or to certified medical centers in routine practice.[8] In Europe, widespread population-based lung cancer screening has so far not been recommended or implemented, as some important issues regarding lung cancer screening still need to be resolved, including the true mortality benefit as compared with that with no screening, harmful side effects, the specification of the optimal screen population, the optimal screen intervals, and the decision regarding a volume- or diameter-based nodule management protocol.[9,10] One additional open question of utmost importance for lung cancer screening programs is how to manage enlarging pulmonary nodules (PNs). Recently, the Fleischner Society updated its recommendations for solid nodules, but its statement concerns only incidental, non-screen–detected PNs. So far, no international society has published a clear recommendations on enlarging PNs.

To address this issue, the advisory board Management of Progressive Pulmonary Nodules Found during and outside of CT Lung Cancer Screening Studies was formed to discuss these questions and formulate consensus statements as the opinion of internationally renowned experts in the field of lung cancer.

Screening and Work-up Alternatives

Lung Cancer Screening: What Can We Expect from Diagnostic Work-up?

Challenges in Lung Cancer Screening. A major concern in the efficacy and cost-efficiency of LDCT lung cancer screening is the false-positive rate. In the NLST, a diameter-based approach was used (maximum diameter of a noncalcified nodule >4 mm). During the first two screening rounds, 27% of those screened had a positive test result, of which only one of 25 results was a true positive.[1] The NELSON study was the first trial to use a volumetric approach in which semiautomated software yielded three-dimensional volume of the detected solid nodules (98% of all nodules).[11] In the case of indeterminate nodules (50–500 mm^3), a short-term follow-up CT (at 3 months in the baseline round) was performed to assess PN growth. If the nodule was fast growing, which is defined as a volume-doubling time of 400 days or less, it was rated as positive (Fig. 1).[12] The two-step approach of volume and growth

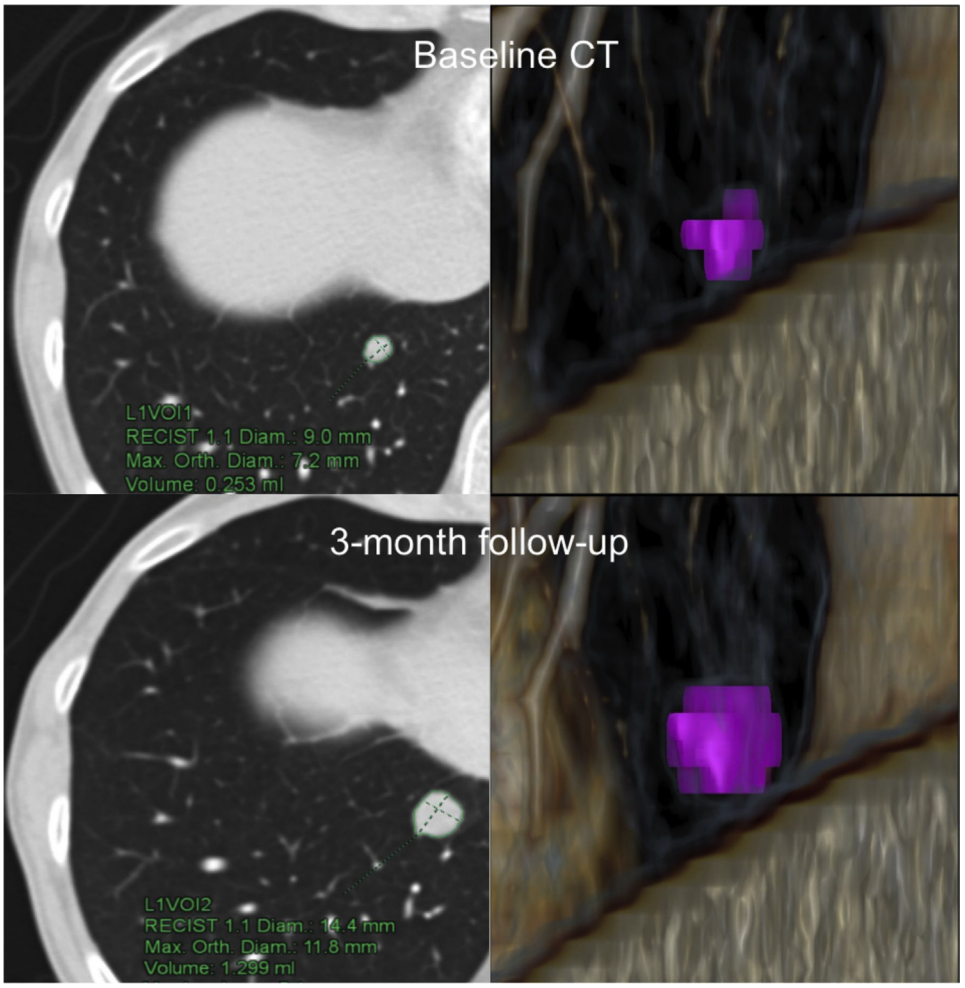

Figure 1. Low-dose computed tomography (CT) scan of a 58-year-old male patient with 67 pack-years of smoking who underwent lung cancer screening. A fast-growing pulmonary nodule with a volume-doubling time of 95 days was detected. An additional positron emission tomography–CT scan showed no malignant uptake in lymph nodes or metastatic disease. The patient underwent anatomical surgical resection and systemic mediastinal lymph node dissection. RECIST, Response Evaluation Criteria in Solid Tumors; Max., maximum; Orth., orthogonal; Diam., diameter.

assessment, resulted in a much lower rate of positive test results compared with that of diameter-based protocols (baseline round 2.6% versus 27% and true positive rate of 36% versus 4%). The negative predictive value was comparable to that of diameter-based protocols.[11] In a recent analysis based on the NELSON results, the initial volume category cutoff values were optimized (Fig. 2).[10]

Work-up after a Positive Screen Test Result. The work-up of screen-detected suspicious PNs at baseline may need to be different from that of new nodules at incident screenings, as these can be expected to be faster growing and are more often malignant.[13] For this reason, follow-up CT to assess growth is performed at a shorter interval in the case of new nodules at interval screenings. Most screen-detected lung lesions are small, peripheral lung nodules.[3] Of the NLST screenees with a positive LDCT result, 90% underwent diagnostic follow-up, with 10% undergoing positron emission tomography (PET)-CT and 5% eventually undergoing biopsy and 4% eventually undergoing an operation.[1] The sensitivity of PET for subcentimeter lung lesions is known to be limited.[14] On the basis of a retrospective analysis of NELSON trial data, a preoperative PET after conclusive work-up results was suggested to reduce the rate of resection of benign lesions.[15] Nearly all lung lesions investigated were less than 3 cm in diameter (mean diameter 15 mm). In these lesions, the diagnostic accuracy of bronchoscopy was limited, with a sensitivity of 13% and negative predictive value of 45%, a very low value of brush or wash (sensitivity 8%–9%), and a 46% sensitivity of endobronchial biopsy.[16] Thus, conventional bronchoscopy cannot be routinely recommended for individuals with screen-detected PNs. Of the NLST and NELSON screenees with a positive screen test result who underwent an invasive procedure including biopsy, 53% (NLST) and 65% (NELSON) turned out to have lung cancer.[11] The role of

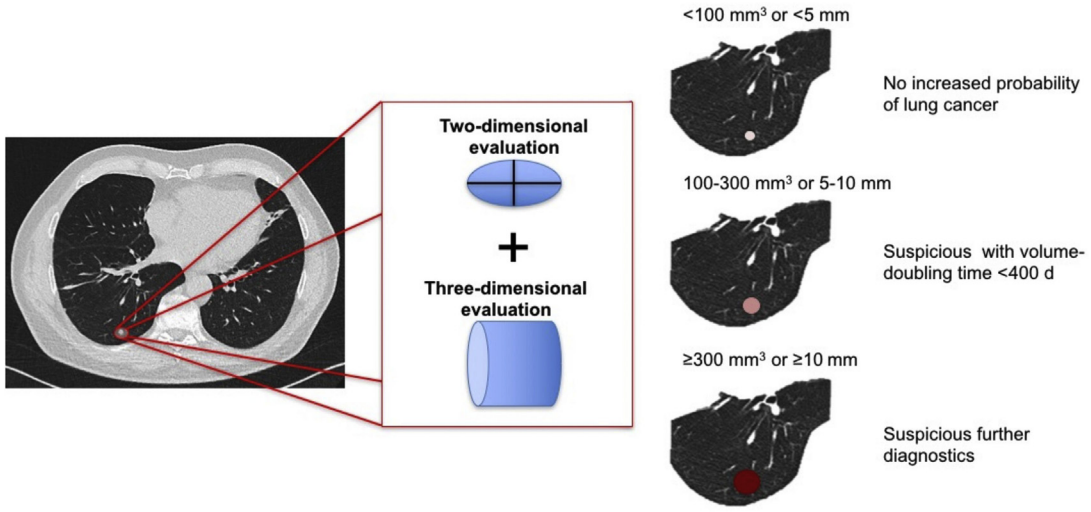

Figure 2. Graphic displaying the optimized cutoff values for screening positive pulmonary nodules according to the findings of the NELSON trail.

CT-guided biopsy in screen-detected nodules remains to be determined in future studies. In a retrospective analysis of CT-guided biopsy in 110 screen-detected nodules, 84% of biopsy results were true positive; the complication rate was 13%.[17] In this analysis, most nodules were larger than 15 mm in diameter.

Surgery: State of the Art and New Surgical Techniques with and without Image Guidance

Surgical excisional biopsy of suspicious nodules remains the diagnostic reference standard for various reasons. The open approach, which allows bimanual palpation and localization of PNs, remains the approach of choice for detection of nodules.

The minimally invasive video-assisted thoracoscopic surgery (VATS) approach is feasible for PNs that are 5 to 50 mm in diameter and located closer to the pleura than their diameter. Smaller nodules and more central nodules may be difficult to find without palpation and may require different localization techniques. The easiest localization technique is insertion of the palpating surgeon's finger through one of the port holes. In cases in which localization difficulties are assumed, preoperative or intraoperative marking of the nodules may be helpful. The markings are commonly achieved with metal hook wires or harpoons that are placed by using CT guidance before resection.[18,19] The main disadvantage of this technique is the physical separation of the CT room and the operating theater.[18,20–22] This limitation may be overcome in a hybrid operating theater setting that includes a manipulator-based, multiaxis, open C-arm interventional suite supporting percutaneous interventions by using cone-beam CT, a three-dimensional laser, and fluoroscopic guidance.[23]

Alternatives to preoperative or intraoperative marking followed by wedge resection are anatomical resection such as segmentectomy and lobectomy. Both can be performed with either minimally invasive techniques (VATS or robotic-assisted thoracic surgery) or an open technique. However, anatomical resections may be associated with a greater loss of functional lung tissue than with wedge resections. This is especially true for lobectomy, which has significantly higher mortality and morbidity rates.[24] Therefore, lobectomies are only exceptionally considered an appropriate technique for excisional biopsy. Segmentectomy can be an alternative to wedge resections as a technique of excisional biopsy for deep-lying nodules because the loss of parenchyma is more limited than with lobectomy and the rate of mortality and morbidity is lower.[24] However, segmentectomies can be technically demanding, especially when performed by VATS or robotic-assisted thoracic surgery, and technical feasibility is dependent on the location of the nodule within the lobe.

All surgical excisional biopsy techniques provide the opportunity for ipsilateral hilar and mediastinal surgical lymph node staging.[25] Intraoperative frozen section can be used to certify malignancy, verify resection margins, and identify the lymph nodes involved (N staging). This rapid (20- to 30-minute) intraoperative histological work-up provides good accuracy when compared with postoperative paraffin embedding tissue work-up (sensitivity of ~94% and specificity of >97%).[26] However, frozen section does have some limitations compared with paraffin embedding.[26]

RT: What Is the Role of SABR and Who Is Eligible?

Technique SABR. Use of modern stereotactic ablative radiotherapy (SABR) (synonymously used term *stereotactic body radiation therapy* [RT]) approaches have

shown beneficial effects on survival in population studies.[27,28] There is sufficient evidence to recommend SABR as the primary therapeutic option for patients with early-stage NSCLC who are medically inoperable or who do not wish to undergo an operation.[29–32] The European Society of Medical Oncology guidelines recommend delivery of a biologically equivalent (tumor) dose of at least 100 Gy prescribed to an encompassing isodose thanks to improved local control and survival.[33] Peripherally located tumors may be treated with short-course regimens including up to five fractions.[34] There is currently no default fractionation regimen in use for moderately central tumors located within 2 cm of the proximal bronchial tree.[35] Nevertheless, it has been shown that short-course regimens such as 54 to 60 (or to 66) Gy in three fractions are associated with an increased risk for toxicity in central tumors.[36,37] Currently available evidence suggests that slightly protracted regimens (from four to 10 fractions) are reasonably safe and effective in more centrally located tumors.[27,35]

Challenges of RT in Comparison with an Operation. *OS Rates.* Compared with conventional radiation techniques, stereotactic approaches provide considerably increased local control rates (~40%–60% versus >85%) and overall survival (OS) rates (~20%–35% versus ~60% at 3 years) in patients who are not eligible for an operation.[27,29,38–40] In medically fit patients (i.e., patients who are commonly treated surgically) survival rates achieved by SABR are considerably higher than those in nonfit patients and comparable to those in surgical series.[28,41,42] The only currently available randomized evidence that directly compared surgery and SABR for early-stage lung cancer is a pooled analysis of two trials that failed to complete accrual (small sample size and inclusion criteria that were not well balanced).[42] SABR alone does not allow lymph node staging (both N1 and N2 nodes), which is recommend in all operable patients.[43] The LACE meta-analysis showed an 11% absolute survival benefit with adjuvant chemotherapy for N1 disease and 16% with N2 disease.[44] Properly designed and powered randomized trials are needed. It is highly recommended that patients be enrolled in ongoing trials comparing resection with SABR, (NCT02468024, ISRCTN13029788, and NCT02984761).

Lack of Pathologically Confirmed Cancer. Preradiotherapy pathological diagnosis is recommended in all patients. However, if tissue sampling is considered associated with inappropriate risk or if the patient decides to refuse an operation (i.e., *informed refusal*), RT can be considered without biopsy.[45,46] Fludeoxyglucose F 18 [FDG]-PET-CT criteria can decrease the likelihood of a benign lesion to less than 4%.[47,48] However, it is generally recommended that a multidisciplinary assessment of the PET/CT scan be performed to determine whether RT should be initiated without pathological confirmation.[27,45] As a threshold value, an 85% likelihood of malignancy (as estimated by various nodule calculators) has been proposed in accordance with recommendations of the International Association for the Study of Lung Cancer.[45,49,50]

Interventional Radiology: Image-Guided Percutaneous Ablative Therapy for PNs?

Patients should be considered for an ablative therapy only when they have advanced tumor stages and/or a reduced state of health, when they have reduced respiratory function, or after all other therapeutic options have been exhausted.[51–53]

Radiofrequency ablation (RFA) and microwave ablation (MWA) are hot thermal ablation techniques, whereas cryoablation is a cold thermal ablation technique. The recently introduced irreversible electroporation (IRE) is considered as a nonthermal ablation technique. MWA has substantial physical advantages over RFA (a lesser heat sink effect, more homogenous and larger ablation zones, and no probe charring) and should thus be the preferred technique.[54] Cryoablation (CA) uses fast freezing and thawing sequences for tissue destruction.

Most published reports are case series, retrospective analyses, or studies with a small sample size.[55] None of the techniques are recommended by current guidelines for early-stage lung cancer. MWA showed promising results in the ablation of lung tumors in general. A clinical success rate of 94% after 15 months has been shown (the rate of pneumothorax requiring a chest tube was 19%).[56] A median OS of 17.7 months and median progression-free survival of 11.8 months in patients with stage IIIB or IV NSCLC who underwent MWA have been reported.[57] A recent study concluded that IRE might be ineffective in the treatment of lung lesions.[58] Data about survival rates after CA are limited. A 2-year progression-free survival rate of 61% to 100% and a 3-year OS rate of 77% to 88% have been reported in cases with early NSCLC.[59,60] The ECLIPSE trial reported a 1-year OS rate of 97% in lung metastasis with sizes of up to 3.4 cm.[55] In terms of safety, a relatively low complication rate for CA of malignant lung tumors has been reported, with 6% of major complications and no Common Terminology Criteria for Adverse Events grade IV or V events.[55,61]

Discussion

General Consensus

After the summary of work-up options for enlarging PNs, it became clear that there is a need for interdisciplinary interaction, as there is a lack of evidence to recommend a specific minimally invasive treatment

approach. All participants agreed that the communication between interventional radiologists, radiation oncologists, surgeons, and other clinicians needs further improvement in quantity and quality and should also include communication of ongoing developments and their potential applications in clinical trials. Furthermore, it became clear that there was a strong general consensus for using FDG-PET-CT as the mandatory primary staging modality for lymph node involvement in patients with increasing PNs on lung cancer screening follow-up, as well as to rule out distant metastatic disease. FDG-PET-CT is already recommended by different guidelines for use in the work-up of NSCLC for staging purposes. There was also a general consensus about the need to better inform fit patients of all therapeutic options available to encourage their involvement in shared decision making.

Lung Cancer Screening

Widespread population-based lung cancer screening in Europe has so far not been recommended or implemented, as some important issues regarding lung cancer screening still need to be resolved as already mentioned. A number of studies have shown that semiautomated or automated volumetric measurement is more reproducible than manual techniques.[10,11] Even more, semiautomated volumetric evaluation has superior sensitivity in the detection of nodule growth.[3,62] In the large majority of cases, volume doubling times for solid cancers are in the range of 100 to 400 days.[11] Using a two-step approach of volume and growth assessment results in a much lower rate of positive test results than does use of diameter-based protocols (baseline round 2.6% versus 27% and true positive rate of 36% versus 4%).[11] Further, it was discussed that double reading may be favorable compared with single reading, as some studies have that shown double reading can improve the rate of PN detection.[63–65] However, it was acknowledged that double reading is not generally used in clinical routine because of limited human resources and cost-effectiveness. Computer-aided detection (CAD) of pulmonary nodules may help address this problem, as the sensitivity (approximately 95%) has improved and may be beneficial in PNs larger than 50 mm^3 compared with a single read alone.[63] However, the evidence for CAD is also limited, and CAD is at this moment not widely used in lung cancer screening evaluation.

Consensus on Lung Cancer Screening. It was agreed in the discussion that a two-step approach of volume and short-term growth assessment should be used in screenees rather than a single diameter approach at a single time point. Cutoff values from the NELSON trial should be used to determine positive and negative findings. However, more data from randomized studies with volume measurements, as well as volume measurements of the existing large United States–based screening trial, are needed to confirm these cutoff values. Double reading and having a validated CAD software algorithm as a "second reader" remain methods to be validated in the future.

Tissue Sampling Approaches and Histological Work-up

Also discussed was the fact that biopsy using the least invasive technique is desirable, as exact histological classification or subclassification will influence treatment decisions. Genetic testing for driver mutations is now routinely recommended in advanced or metastatic disease.[66] These mutations, when present, will guide treatment decisions in inoperable patients, as well as in those who have a relapse after radical treatment. However, the true therapeutic benefit in early-stage disease is not yet clear.[67] An adequate amount of tissue should be acquired to perform accurate histological and, in some specific cases (e.g., multiple nodules), molecular characterization. There are different approaches, including sputum cytological examination, navigational bronchoscopy, endobronchial ultrasound (EBUS)-guided lung biopsy, transthoracic fine-needle aspiration, EBUS with fine-needle aspiration, or biopsy, pleural fluid cytological examination, and pleural biopsy. If these procedures fail to generate adequate tissue material, a surgical biopsy (e.g., by VATS) is recommended. In principle, the nodules will mostly be N0 lesions according to PET and CT criteria. Therefore, the role of EBUS/endoscopic ultrasound (EUS) would be limited to lesions that are immediately adjacent to the central airway/esophagus or those with suspected N2 involvement.

Consensus on Tissue Sampling Approaches and Histological Work-up. The approach to biopsy of progressive PNs should be chosen according to the current guidelines, with use of the least invasive technique. Individual risk assessment is needed in every patient and should take into account the likelihood of obtaining sufficient diagnostic material, the location of the PN, and the potential complications of the proposed procedure. Future studies should evaluate the sufficiency of tissue sampling of individual minimally invasive approaches. It was agreed that a full pathological work-up of each tissue sample is needed in patients with positive lymph nodes or advanced disease. This should include *EGFR* activating mutations and *ROS1* or ALK receptor tyrosine kinase gene (*ALK*) rearrangements, as well as programmed death ligand 1 testing. In patients with a singe lesion and no lymph node involvement, a full pathological work-up may not be necessary, depending on the country-specific guidelines. To minimize processing

time, the pathological work-up should be performed locally in each center, with only specific molecular evaluations performed in a dedicated center.

Surgery

Surgical excisional biopsy should always be considered in cases in which less invasive procedures fail and the level of clinical suspicion of lung cancer is high (Brock calculation >10%[50]). If an intraoperative frozen section confirms that the lesion is a lung cancer, the appropriate anatomical resection (usually lobectomy) in association with a systematic lymph node dissection can deliver definite curative treatment in a single procedure in early stages. Excisional biopsy, as well as completion lobectomy, should be performed by using a minimally invasive technique whenever possible, even for tumors smaller than 2 cm, provided that the surgical procedure (including the lymph node dissection) is performed to the same standard as with an open technique. However, current trails are investigating segmentectomy versus lobectomy in tumors smaller than 2 cm that are located in such a manner as to allow this technique to offer an R0 resection. Systematic lymph node dissection is mandatory per the current European guidelines,[25] especially in the light of the upstaging rate of up to 20% because of surgical staging of the mediastinum.

Consensus on Surgery. Surgical excisional biopsy should be offered in all unclear cases or cases with a high suspicion of malignancy. Minimally invasive techniques and parenchyma-sparing techniques are desirable. Intraoperative histological examination followed by subsequent anatomical resection is feasible. Until proved otherwise, lobectomy remains the therapy of choice. Systematic lymph node dissection is the only acceptable nodal staging method.[25]

Specific Issues—Wire-Guided Surgery

After discussion in the multidisciplinary tumor board (MDTB), the most appropriate diagnostic surgical modality for suspicious screen-detected small and/or deep intraparenchymal lung lesions or ground glass opacities is one-step surgical removal for diagnostic and therapeutic purposes, preferably after CT-guided wire placement (for a PN >1 cm) unless severe comorbidity prohibits surgery. Guide wire placement using a hybrid theater seems to be beneficial.[23] If the lesion is proved to be an invasive lung cancer, the most suitable definitive treatment modality should be determined in a multidisciplinary setting.

Consensus on Wire-Guided Surgery. Minimally invasive resection with guide wire placement for localization is recommended for lesions with a depth-to-diameter ratio greater than 1 or ground glass opacities with expected localization difficulties.

RT

Highly conformal modern RT approaches (SABR) have shown beneficial effects on survival and toxicity in several nonrandomized studies, leading to sufficient evidence for recommendation of SABR as the primary therapeutic option for patients with early-stage NSCLC who are medically inoperable or who do not wish to undergo an operation. Currently, however, there are no sufficiently powered studies directly comparing surgery with SABR. The limitation of SABR is the toxicity of radiation, including pneumonitis, bronchial stenosis, and esophagitis.

Consensus on RT. It was agreed that SABR is a promising therapeutic approach. However, it should be implemented only in those patients with progressive PNs, in cases in which surgery is high risk, or if the patient refuses an operation, as there is a lack of studies supporting an equivalent OS in comparison with surgical resection. This decision could be made according to the European Respiratory Society/European Society of Thoracic Surgeons (ESTS) guidelines on fitness for radical therapy.[68] SABR protocols should be adapted to current guidelines. After SABR, a follow-up visit including a chest CT, medical history, and physical examination is recommended at least every 6 months for 3 years. Future results from the VALOR trial and SABRTooth trial, which are assessing patients with Stage I lung cancer who are randomized to receive SABR or an operation, may change current recommendations. It is highly recommended that patients be enrolled in ongoing trials comparing resection with SABR in early-stage lung cancer (e.g., NCT02468024, ISRCTN13029788, and NCT02984761).

Interventional Radiology

Four main minimally invasive approaches were discussed: RFA, MWA, CA, and IRE. RFA was evaluated as a primary therapeutic option for primary NSCLC in patients who are not eligible for subsegmental resection or lobectomy. Limitations of this technique for solid tumor ablation in the lung are tumor size and proximity to blood vessels.

Consensus on Interventional Radiology. It was agreed that at the moment there is no evidence for these techniques in a curative treatment setting of malignant enlarging PNs. However, RFA or MWA can be considered in those patients in whom an operation and SABR cannot be tolerated, in cases of one or two lesions, tumor

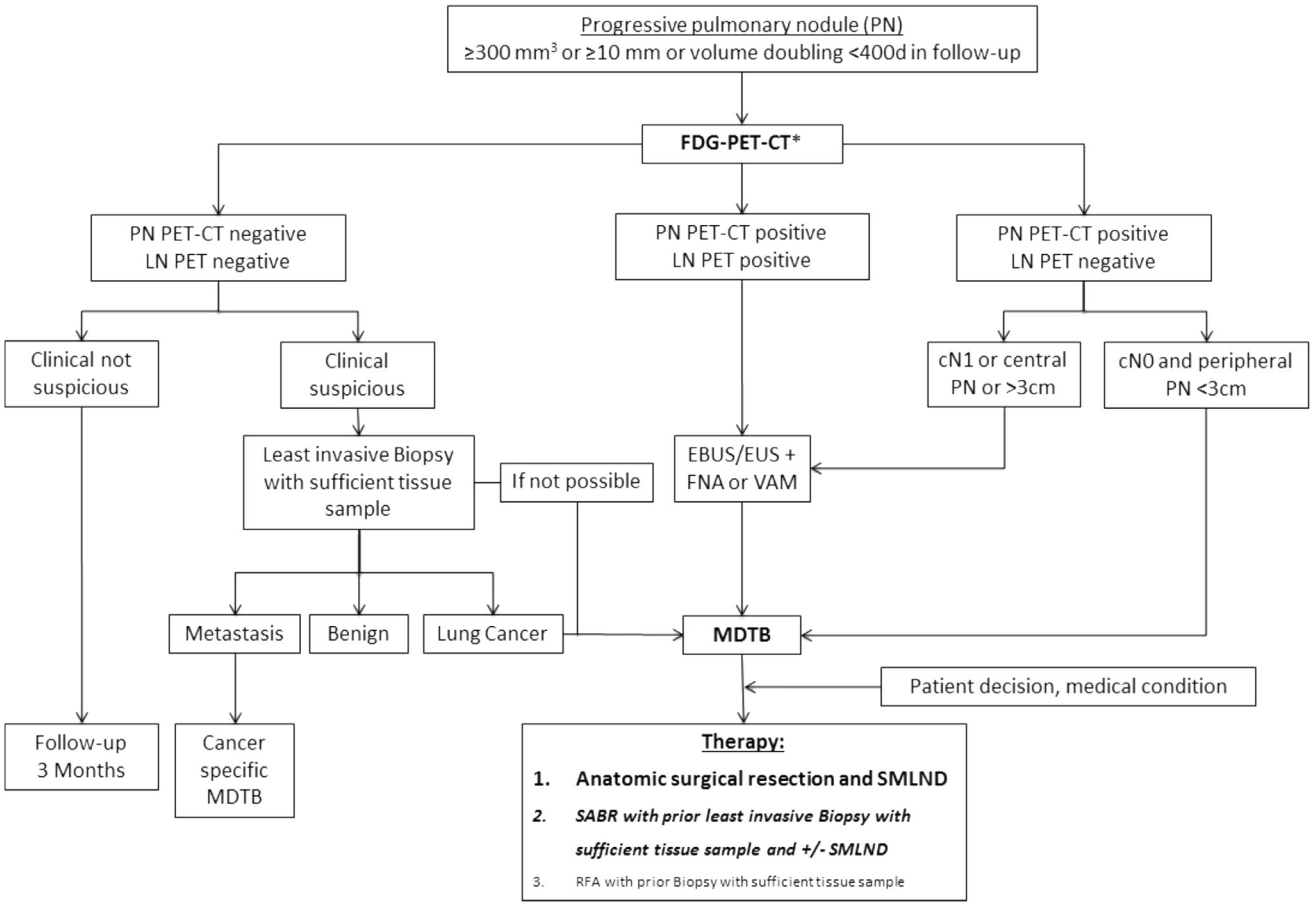

Figure 3. A proposed work-up of progressive lung nodules as agreed on at the Dresden 2015 Post-World Congress of Lung Cancer/International Association for the Study of Lung Cancer Workshop. *For N and M staging positron emission tomography (PET), negative pulmonary nodules smaller than 1.5 cm should still considered positive because of screening progress and the limited value of PET in nodules smaller than 1.5. Abbreviations: FDG-PET-CT, fludeoxyglucose F 18 PET-computed tomography; PN, pulmonary nodule; LN, lymph node; EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound; FNA, fine-needle aspiration; VAM, video-assisted mediastinoscopy; MDTB, multidisciplinary tumor board; SMLND, systemic mediastinal lymph node dissection; SABR, stereotactic ablative body radiotherapy; RFA, radiofrequency ablation.

smaller than 2 cm, and slow-growing disease. Follow-up with standard CT should be performed after 6 months at the earliest and by FDG-PET not earlier than after 3 to 6 months to minimize false-positive findings after RFA. There was no recommendation for MWA, CA, or IRE in early-stage lung cancer in medically operable patients.

Specific Issues—Mediastinal Lymph Node Biopsy

Accurate preoperative staging including histological examination of mediastinal lymph nodes should be considered in patients with resectable progressive PNs.[43] It was pointed out by the board that there is a lack of adequate mediastinal lymph node staging in enlarging PNs. This may lead to a false preoperative staging resulting in inadequate therapy regimens. Mediastinal lymph node biopsy can be performed by either EBUS/EUS with fine-needle aspiration or video-assisted mediastinoscopy, depending on the size of the lung cancer and a finding of positive lymph nodes on FDG-PET-CT. The mediastinal lymph node assessment should be carried out in accordance with the current European guidelines (67).

Consensus on Mediastinal Lymph Node Biopsy. The board agreed that mediastinal lymph node evaluation (at the very least, stations 4 and 7) is mandatory in each patient with increasing PN before treatment in a curative setting. It was discussed that the combined use of endoscopic staging and surgical staging is preferred, as it results in a higher accuracy as recommended by the ESTS guidelines.[69] In particular, when there are no enlarged lymph nodes on CT or no uptake in lymph nodes on FDG-PET CT, direct surgical resection with systematic mediastinal lymph node dissection is indicated for PNs that are 3 cm or larger and located in the peripheral lung. In centrally located PNs or those with N1 nodes on FDG-PET or CT, preoperative invasive mediastinal staging is indicated. As with lung cancer detected outside of screening programs, the choice

between endoscopic staging with EBUS/EUS and fine-needle aspiration or video-assisted mediastinoscopy in progressive PNs depends on local expertise and should be conducted as described in the current ESTS guidelines.[69]

Specific Issues—MDTB

Adequate treatment plans can be developed only when expert teams of oncologists, surgeons, radiation oncologists, a radiologist, and a pulmonologist discuss each patient in a multidisciplinary tumor board (MDTB). The board pointed out that there is a lack of discussion of patients with progressive PNs in a MDTB. This may lead to underestimation of sufficient and new therapeutic approaches and lack of inclusion in ongoing trials. Further, there is a lack of standardized reporting and sharing of the MDTB reports. An individually tailored approach for each center has to be considered.

Consensus on MDTB. It was agreed that each patient with an enlarging nodule, as defined earlier, has to be discussed in an MDTB both to determine the best diagnostic pathway and for definitive management, as the patient may benefit from ongoing development and trials. It was pointed out that MDTB reports should be more standardized and structured to include as much information as possible. It was further agreed that each individual center should collect its local rates of benign diseases (e.g., tuberculosis) before discussion of therapeutic actions.

Conclusion

This interdisciplinary advisory board concluded that FDG-PET-CT and preoperative mediastinal lymph node evaluation are essential diagnostic steps in evaluating patients with enlarging PNs (Fig. 3). Each patient should be discussed individually in an MDTB, taking into account patient condition, comorbidities, likelihood of cancer, local population rate of benign PNs, etc. As the first-line therapeutic option, surgery should be considered. SABR should be considered in patients not eligible for an operation. At the moment, there is no evidence for invasive interventional radiology approaches. Future large randomized studies on SABR and minimally invasive therapeutic procedures are needed in order to consider them primary alternatives to surgery.

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