Transthoracic Needle Biopsies: It’s More than Just Hitting the Bull’s-eye

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Summary:

Spectroscopy has shown to be of value in determining benign from malignant tissue.

Incorporation of spectroscopic measurements may increase the diagnostic yield of transthoracic needle biopsies. Given the increasing amount of incidentally found lung lesions, such a technique may prevent unnecessary invasive procedures and uncertainty for the patient.
In this issue of *Clinical Cancer Research*, Spliethoff et al. describe the feasibility of an innovative technique with a spectral tissue sensing probe at the tip of a biopsy needle during transthoracic needle biopsies of lung lesions (1). They show that the biopsy needle could guide the interventional physician to the region of interest to increase the diagnostic yield of the procedure. The scientific background of diffuse reflectance spectroscopy in discriminating benign form malignant disease has been described before and is supported by clinical data (1, 2). In the present paper Spliethoff et al. translate this knowledge into a clinical applicable technique, which has potentially major clinical impact. Although the number of patients investigated at present is small with only 11 cases during transthoracic needle biopsies, the technical aspects of the needle together with the limited duration of the procedure do support broader applicability.

The widespread use of computer tomography of the thorax in the diagnostic workup for different kind of diseases, inherently cause a growing number of incidental findings, causing diagnostic problems. One of the most frequent found lesions are solitary pulmonary nodules (SPN). A SPN is defined as a single, discrete pulmonary opacity that is surrounded by normal lung tissue and is not associated with adenopathy or atelectasis. These SPN do represent a major diagnostic problem as without a histological tissue diagnosis the origin and fate are uncertain.

Also due to the introduction of computer tomography lung cancer screening in different part of the world including the United States a growing number of SPN are detected (3). One of the major concerns with lung cancer screening is the high number of false positive findings, defined as SPN without clinical meaning. In the national lung screening trial over 95% of patients who underwent thoracic surgery for a SPN with unknown pathology, ultimately were diagnosed with benign disease (3).
To decrease the number of false positive findings a number of algorithms have been developed and are used in screening programs (4,5). In the Dutch-Belgium NELSON trial volumetric assessments are used in repetitive scans, to determine growth of a lesion (4). This volume doubling time calculation is then used to estimate the change of a SPN being malignant. Another frequently used algorithm is the solitary nodule risk calculators (SPN calculators). Based on the patient characteristics, the aspects of the lesion, etc, the computer calculates the risk of the SPN to be lung cancer (6).

The key issue remains whether an individual patient will accept that his or her diagnostic workup is based on risk calculation and what is the psychological impact on a patient of the knowledge of having a SPN without a clear diagnosis. Certainly this is the case in these patients who a priori have a higher change of malignancy such as current or former smoker, which are the current inclusion criteria for lung cancer screening. In these individuals, fit enough to undergo treatment, it is questionable whether patients are willing to accept to postpone further workup and diagnostics based on these algorithms. Whether the delay in diagnostics really has an impact on the prognosis of the patient is a matter of debate and further investigation (7).

Apart from this, based on risk calculation without pretreatment pathological sampling, there is an increasing usage of stereotactic irradiation for SPN in non-surgical patients or because of patient preference. This will increase the population of patients treated without a histological diagnosis, as no resection will take place. This ultimately causes an increase of the population who have the stigma of being lung cancer patient with the accompanying follow up, but for a benign disease.

The introduction of advanced imaging techniques like PET-scanning will certainly be off additive value but sensitivity and specificity issues remain.
All the above mentioned arguments underline the need for proper histopathological diagnosis of lung lesions in a minimal invasive way. To obtain pathological specimens in general a bronchoscopy or a CT-guided biopsy are performed. The diagnostic yield of bronchoscopy for small peripheral lesions is low (8) and in these patients in general a CT-guided transthoracic needle biopsy is performed. Although relatively safe with pneumothorax and pulmonary bleeding as major concerns a diagnostic yield of the biopsy is in need for improvement.

It should be clear for interventional pulmonologists and radiologists that it is not only about reaching the lung lesion but also reaching a part of the lesion which yields a diagnosis. It is not only about reaching the bull’s-eye but also making the leg. One of the main reasons for a non diagnostic needle biopsy apart from not reaching the lesion is the fact that the number of viable cells is to limited to obtain proper diagnosis. In case of a malignancy as cause for a lung lesion the lesion consists of viable malignant cells, necrosis, stromal cells, immune cells, and blood vessels (Figure 1). Proper guidance of the needle to derive a biopsy from a viable tumor part will increase the diagnostic yield.

Spliethoff et al. show that guidance by DRS was able to guide the radiologist to a viable part of the tumor (1). In the present study the population of patients included is small and all patients were diagnosed with lung cancer. More data are needed in patients with other diseases like other malignancies or benign diseases. The authors did not discuss how they anticipate taking this technique forward to pave the road for broader clinical introduction.

The question remains whether the spectroscopy on its own ultimately can replace pathology. At present no robust data on positive or negative predictive value are present in this setting and therefore this discussion is premature. However from the spectroscopic data
information beyond pathology can be obtained. Whether light is scattered or absorbed by
the tissue, depends on tissue composition (1,9). Analysis of the tissue’s spectral response to
illumination will provide specific quantitative morphologic, biochemical, and functional
information (1,9). In the present analysis Spiethoff et al. limit the analysis of the spectrum to
an index defined as the relative difference in the water-to-scattering ratio between tumor
and lung tissue within the same individual. (1). From the spectra additional information may
be obtained which will open the field investigating physiological data of the tumor and its
tumor milieu. In an earlier study we found with optical spectroscopy differences in tumor
hypoxia in lung cancer, which was suggested to be prognostic (9).

Although we only at the beginning of analyzing the impact of these factors and
therefore can only speculate, knowing the physiological state of the tumor and it milieu may
have influence forthcoming treatment decisions.

The study of Spiethoff et al. is an important study as it may increase the diagnostic
yield of CT-guided biopsies of lung lesions. This is clinically relevant given the number of
lesions without pathological prove. The spectroscopic technique used opens a wide field of
in vivo physiological analysis of the tissue, which may provide important additional
information. Further implementation of the technique will depend on its value in a larger
population of patients with different kind of diseases.

References

1 Spiethoff JW, Prevoo W, Meier MAJ, de Jong J, Evers DJ, Sterenborg HJCM, et al. Real-time in
vivo tissue characterization with diffuse reflectance spectroscopy during transthoracic lung


Figure 1. Biopsy of a tumor and tumor tissues

A, transthoracic needle biopsy, illustrating a lung lesion. B, magnification of a malignant lesion showing in blue normal tissue surrounding the invasive border of the tumor. The tumor consists of necrotic fields (gray lines) surrounded by avital tissue in black. The necrotic and avital tumor tissue is nondiagnostic at puncture. Blood vessels invade the tumor tissue. C, further magnification of a vital part of the tumor showing that the tumor tissue is build up from cancer cells in blue, immune cells in gray, stromal cells in black, and blood cells in red. Only in case of enough tumor cells the biopsy will be diagnostic.
Figure 1:

Target of biopsy

- Rim of the tumor
- Normal tissue
- Necrotic part
- Avital cells
- Cancer cells
- Blood vessels
- Immune cells
- Stromal cells

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