DIFFERENCE IN STRAIN ELASTOSONOGRAPGY BETWEEN BENIGN AND MALIGNANT PERIPHERAL PARENCHYMAL LUNG LESIONS

Document date: 16th November 2022

INTRODUCTION

Ultrasonography has been widely used for diagnosis since it was first introduced in clinical practice in the 1970s. For lung assessment, ultrasonography is not frequently used in medical practice.(1)

Lung has long been thought to be an organ that cannot be examined by ultrasonography due to its high air content (>90%), which blocks the ultrasonic signal due to the large acoustic impedance differential between the superficial tissues of the chest.(2)

In recent years, the use of lung ultrasonography has expanded beyond emergency situations to include routine examinations of patients with chronic lung illnesses. Lung ultrasonography has several benefits, including cheap cost, real-time imaging, and the lack of radiation.(3)

Elastography was developed in the 1990s to map tissue stiffness and reproduce/replace the palpation performed by clinicians. Two main types of elastography are currently in use, strain elastography where the tissue displacement in response to gentle pressure is used to compute and image tissue

strain, and shear wave elastography where the speed of shear wave traversing tissue is measured and used to create an image of tissue stiffness.[4, 5]

Elastosonography has been used to assess tissue stiffness and elasticity, particularly in liver, thyroid, breast, and prostate nodules suspected of cancer are currently investigable organs for non-invasive diagnostic imaging.[6, 7]

The form, echogenicity, shadowing, and regularity of the margin are all factors to consider when assessing solid lesions with ultrasound. Thoracic ultrasound can also detect most of pleural pathologies e.g., effusion, pneumothorax, pneumonia, or bronchopneumonia consolidations in the subpleural zones, as well as local thickening (3 mm) of the pleural line.[8]

Lung ultrasound wave elastography (LUSWE) approach has the capability of assessing superficial lung tissue stiffness safely and swiftly with the objective of providing a noninvasive tool for evaluating lung elasticity.[9]

The lung surface includes the space between the parenchyma and intercostal muscles; the surface wave speed on the lung is contributed by both the lung and the muscle.[10]

Direct vibration stimulation on the lung surface is not achievable during lung testing. A vibration stimulation on the chest wall causes surface wave propagation on the lung.[11]

An ultrasonic probe is used to detect the propagation of the tissue wave motion (usually a few micrometers). By indenting a medium and examining the

relationship between the indentation displacement and the generated force, the indentation technique may determine the elasticity of that medium.[12]

A local mechanical vibration on the chest safely generates the surface wave on the lung in LUSWE. Diagnostic ultrasonography is only utilized to identify the propagation of surface waves on the lung. Strain pictures are created by repeatedly applying modest pressure to the tissues using the transducers.[13, 14]

Following tissue movement is tracked between pairs of echo frames, and strain is determined based on the axial gradient of the displacements. A stiff area endures less strain (deformation) than surrounding softer tissue when subjected t o the same amount of force.[9, 15]

Most hospitalized patients are not able to perform radiological imaging either due to unavailability or inability to ambulate the patients for imaging to be held. We suggested to perform bedside, relatively cheap and available, imaging modality to help in the differentiation between benign and malignant peripheral lung pathologies.

Lung elastography, to be used as diagnostic tool, is considered a new era worldwide; a new modality that will help to reduce the burden and the widespread use of chest computed tomography.[16]

AIM OF THE WORK

The aim of this study is to demonstrate the applicability and efficacy of strain elasto-sonographic measurements in differentiating between benign and malignant peripheral parenchymal lesions.

PATIENTS

This study will include patients recruited in cross-sectional sample till achieving requirement of 120 patients with benign and malignant subpleural parenchymal lesions.

Sample size was calculated by medical research institute and biomedical informatics, Medical Statistics Department, Alexandria University.
(APPENDIX A)

Patients enrolled in our study will be examined and investigated in chest department, in Alexandria Main University Hospitals.

Inclusion criteria:

1) Adult patients above age of 18 years old.
2) Patients with peripheral lung lesion.

Exclusion criteria:

1) Pure pleural lesions.
2) Clinical instability to reach the final diagnosis.
3) Inaccessibility by ultrasound.

METHODS

This is a diagnostic accuracy study with comparison to gold standard tests e.g., chest computed tomography, transthoracic biopsy, or microbiological analysis. All patients included in this study will give informed consent according to the guidelines of ethics committee, Alexandria Faculty of Medicine. (http://www.med.alexu.edu.eg/wp-content/uploads/2012/04/Checklist-FINAL-20141.pdf-)

Informed consent is available at (http://med.alexu.edu.eg/alexuniv/wp-content/uploads/2021/09/Standard-Operating-Procedure-2020-ethics.pdf).

All patients will be subjected to:

1) Thorough history taking.
2) Complete physical examination.
3) CT scan chest.
4) Routine laboratory investigation profile.
5) Conventional methods to reach final diagnosis such as microbiological analysis, CT scan, fiberoptic bronchoscopy, and image guided biopsies.
6) Strain elastography done by superficial and deep probes, in which B mode is compared with the elastography image for real time assessment; strain ratio is obtained. Strain ratio between benign and malignant peripheral lung lesions to be evaluated.

Data collected from our research aim to estimate a cut-off value by which benign and malignant peripheral parenchymal lesions to be easily discriminated by ultrasonographic elastography.

Statistical methods:

Considering nominal data e.g., clinical features, CT findings, epidemiology, smoking status, and final diagnosis will be statistically analyzed using median, mode, MANN-WHITNEY, and Chi square tests.

While numerical data analysis as arithmetic mean is helpful in situation of age statistical distribution. Strain ratio interpretation, the telltale sign of our study, is directed towards comparison of the cut off value achieved with the final diagnosis of the patients.

Receiver operator characteristic (ROC) curve will be plotted to evaluate and assess the sensitivity and specificity of strain ratio obtained from elastography compared to final diagnosis for 60 of our patients from the total 120 patients recruited in the study.

While according to the remaining 60 patients, a multivariate Cox proportional hazard analysis would be held to validate and evaluate results obtained from the former 60 examined patients.

At the end of the study, sensitivity, specificity, area under the curve (AUC), accuracy of a certain cut-off value, positive predicted value (PPV) and negative predicted value (NPV) would describe the performance of strain ratio as a diagnostic tool in the main aim of the research.

ETHICS OF RESEARCH

Research on human or human products:

☐ Prospective study: Informed consent will be taken from patients. In case incompetent patients, the informed consent will be taken from the guardians.

☐ Retrospective study: Confidentiality of records will be considered

☐ DNA / genomic material: Informed consent for DNA / genomic test and research will be taken from patients. No further tests will be carried out except w further approval of committee and patients. If the samples will travel outside Egy the researcher will be responsible for transportation and security approval.

☐ All drugs used in the research are approved by the Egyptian Ministry of Health

---

Research on animal:

☐ The animal species are appropriate for the test.

☐ After test, if the animal will suffer, it will be euthanized and properly disposed.

☐ After operation, it will have a proper postoperative care.

سأقوم بتسليم الموافقات المبنية على علم المريض الخاصة بالدراسة عند الانتهاء منها او عند طلبها من اللجنة

RESULTS

The results obtained from this study will be tabulated and statistically analyzed using appropriate statistical methods and appropriate figures and diagrams.

DISCUSSION

The results obtained from this study will be discussed in the view of achievement of the aim and will be compared with any of the available published data in the same field of the research.

REFERENCES

1. Beach KW. 1975-2000: a quarter century of ultrasound technology. Ultrasound Med Biol. 1992;18(4):377-88.

2. Volpicelli G. Lung sonography. J Ultrasound Med. 2013;32(1):165-71.

3. Marini TJ, Rubens DJ, Zhao YT, Weis J, O'Connor TP, Novak WH, et al. Lung Ultrasound: The Essentials. Radiol Cardiothorac Imaging. 2021;3(2):e200564.

4. Sigrist RMS, Liau J, Kaffas AE, Chammas MC, Willmann JK. Ultrasound Elastography: Review of Techniques and Clinical Applications. Theranostics. 2017;7(5):1303-29.

5. Gennisson JL, Deffieux T, Fink M, Tanter M. Ultrasound elastography: principles and techniques. Diagn Interv Imaging. 2013;94(5):487-95.

6. Hairu L, Yulan P, Yan W, Hong A, Xiaodong Z, Lichun Y, et al. Elastography for the diagnosis of high-suspicion thyroid nodules based on the 2015 American Thyroid Association guidelines: a multicenter study. BMC Endocrine Disorders. 2020;20(1):43.

7. Barr RG. Elastography in clinical practice. Radiol Clin North Am. 2014;52(6):1145-62.

8. Sperandeo M, Trovato FM, Dimitri L, Catalano D, Simeone A, Martines GF, et al. Lung transthoracic ultrasound elastography imaging and guided biopsies of subpleural cancer: a preliminary report. Acta Radiol. 2015;56(7):798-805.

9. Boccatonda A, Susca V, Primomo GL, Cocco G, Cinalli S, Di Resta V, et al. Role of shear-wave and strain elastography to differentiate malignant vs benign subpleural lung lesions. Medicine. 2021;100(1):e24123.

10. Suki B, Stamenović D, Hubmayr R. Lung parenchymal mechanics. Compr Physiol. 2011;1(3):1317-51.

11. Zhou J, Zhang X. Effect of a Thin Fluid Layer on Surface Wave Speed Measurements: A Lung Phantom Study. J Ultrasound Med. 2019;38(5):1361-5.

12. Zhang X, Osborn T, Zhou B, Meixner D, Kinnick RR, Bartholmai B, et al. Lung Ultrasound Surface Wave Elastography: A Pilot Clinical Study. IEEE Trans Ultrason Ferroelectr Freq Control. 2017;64(9):1298-304.

13. Wells PN, Liang HD. Medical ultrasound: imaging of soft tissue strain and elasticity. J R Soc Interface. 2011;8(64):1521-49.

14. Diao X, Zhu J, He X, Chen X, Zhang X, Chen S, et al. An ultrasound transient elastography system with coded excitation. Biomed Eng Online. 2017;16(1):87.

15. Dietrich CF, Barr RG, Farrokh A, Dighe M, Hocke M, Jenssen C, et al. Strain Elastography - How To Do It? Ultrasound Int Open. 2017;3(4):E137-e49.

16. Zhou B, Yang X, Zhang X, Curran WJ, Liu T. Ultrasound Elastography for Lung Disease Assessment. IEEE Trans Ultrason Ferroelectr Freq Control. 2020;67(11):2249-57.

APPENDIX A

Alexandria University
Medical Research Institute
Biomedical Informatics&
Medical Statistics Department

Name: Dr Ahmed Farag

Sample Size Calculation

The main aim of this study is to demonstrate accuracy of elastosonographic measurements in differentiating benign vs malignant subpleural parenchymal lesions compared to clinical, radiological (CT/PET). A recent study concluded that the ROC curve elaborated for the diagnosis of malignancy by strain elastography showed an AUC of 0.688. [1] Consequently, patients will be recruited in a cross-sectional sample till achieving the minimum required sample of 60 patients with benign vs 60 patients with malignant subpleural parenchymal lesions with 80% power.

Sample size was calculated using a two-sided, ROC curve test at .05 significance level using R software.

Program Citation:

R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

Reference:

Boccatonda, A., Susca, V., Primomo, G. L., Cocco, G., Cinalli, S., Di Resta, V., Martino, L., Mucilli, F., Marinari, S., Cipollone, F., & Schiavone, C. (2021). Role of shear-wave and strain elastography to differentiate malignant vs benign subpleural lung lesions. Medicine, 100(1), e24123. https://doi.org/10.1097/MD.0000000000024123

Calculated and reported by: Dr Iman El Sayed
Assistant Professor of Medical Statistics, systematic reviews and Evidence Synthesis. Medical Statistics Department, Medical Research Institute-Alexandria University
Email: Eman.abd.elftaah@alexu.edu.eg. Linkedin: *www.linkedin.com/in/imanelsayed83,*
Tel: +201116631103

Dr Iman El Sayed
26/3/2022

جامعة اسكندرية
معهد البحوث الطبية
قسم المعلوماتية الحيوية والأحصاء الطبي