Original Article

Presence of Color Transition in Biopsy Specimens Predicts Outcome of Liver Lesion Biopsies

Fleur Sophie Gittinger*, Laura Wetterich, Patrick Michl, A. Cristina Ripoll

Martin-Luther Universitätsklinikum Halle-Saale, Klinik für Innere Medizin I, Halle- Saale, Germany Universitätsklinikum Jena, Klinik für Innere Medizin IV, Jena, Germany

Abstract

Background: The aim of this study was to evaluate the usefulness of the presence of tissue transition in liver lesion biopsies to predict a successful outcome, as observed by modified macroscopic on-site evaluation (MOSE). **Methods:** This is a retrospective analysis of 264 ultrasound-guided liver lesion biopsies, examining the influence the presence of tissue transition (visible color changes in biopsy specimens as evaluated visually) has on two endpoints (1) material retrieval, (2) attaining a definitive diagnosis) representing successful liver lesion biopsies, compared to previously evaluated variables in this context. Uni- and multivariate analyses were performed using SPSS 21.0. **Results:** Material retrieval and a definitive diagnosis occurred in 224/264 (84.8%) and 217/264 (82.2%) cases, the latter occurring more often when visual inspection revealed macroscopic tissue transition (92/96 [95.8%]) than when not (124/165 [75.2%]), $P < 0.001$. Tissue transition in biopsies was more common in secondary (74/162 [45.7%]) than (18/54 [33.3%]) primary liver lesions, though this was not significant ($P = 0.112$). On multivariate analysis, tissue transition in biopsies was an independent predictor of a definitive diagnosis and material retrieval. **Conclusion:** In liver lesion biopsies, MOSE of color transition in biopsies can indicate success. This is easily incorporated into clinical practice and can help overcome the lack of an on-site pathologist.

Keywords: Color transition, liver lesion biopsy, macroscopic on-site evaluation

Introduction

Ultrasound-assisted liver biopsies are a safe, routinely used method to obtain tissue samples for diagnosing diffuse and focal liver diseases and to guide disease management. In biopsies of focal liver lesions, the number of inconclusive biopsies has been reported to be higher (7.1%) than compared to parenchymal biopsies (1.7%), although this depends on how a conclusive or inconclusive biopsy is defined.[1] So far, a number of factors influencing the outcome of a biopsy have been identified for both diffuse and focal liver diseases.[1-6] These have focused mainly on technical aspects such as type and size of the needle or on aspects regarding the lesion itself such as size, histology, or location of the lesion within the liver with varying results.[1,5,7] Indeed, among the variables evaluated (needle gauge or type, number of passes, lesion characteristics such as location, size, or histology), only tumor visibility on ultrasound significantly predicted a successful outcome.[1,5,8,9] Nevertheless, there are other aspects which have not been evaluated, namely the presence of macroscopic tissue transition of the biopsy specimen as observed visually. If material other than normal liver tissue has been retrieved, a macroscopically visible tissue transition can be present, represented as a color transition from yellow-brown liver tissue to, in the case of some metastatic lesions, white tissue. This easy to recognize sign may be well known to experienced physicians and can give the examiner information on whether the lesion has been targeted correctly. Recently, macroscopic on-site evaluation (MOSE) has been proposed as a method to evaluate the adequacy of a specimen obtained by endoscopic ultrasound-guided fine-needle biopsy and to help overcome the lack of an on-site pathologist.[10] It could be shown that specimens with a macroscopic visible core ≥4 mm on MOSE

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Address for correspondence: Dr. Fleur Sophie Gittinger, St. Georg Clinic, Department for Gastroenterology, Hepatology, Diabetology and Endocrinology, Delitzscher Str. 141, 04129 Leipzig.
E-mail: fleursophie.gittinger@sanktgeorg.de

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can improve diagnostic yield by indicating the specimen's adequacy.[10] Therefore, the aim of this study was to evaluate the use of the presence of tissue transition as observed by MOSE to predict the attainment of a definitive diagnosis in a liver lesion biopsy.

Methods

This study is a retrospective cross-sectional, monocentric study involving biopsies performed at the ultrasound department of the Martin- Luther University Clinic Halle (-Saale), between January 01, 2016, and December 31, 2019. Cases were identified from a preexisting database of all interventional procedures performed in the ultrasound unit. The original MOSE included, besides the observation of a tissue transition, the length of the tissue with a different color.[10] For the present study, a modified MOSE was applied, in which MOSE incorporated the evaluation of a macroscopically visible change in color in the tissue of the biopsy specimen, representing both peripheral liver tissue and the lesion biopsied. Ideally, the biopsy specimen contained both types of tissue in equal measure. This tissue transition can occasionally be associated not only to a change in color but also to a change in texture of the biopsy specimen [Figure 1].

Ultrasound-guided biopsy technique

The liver was scanned with a 3.5 MHz curved array ultrasound probe (Canon Medical Systems) and biopsies were performed using a 3.5 MHz curved array probe with an integrated guide system (Canon Medical Systems). Ascites prior to any puncture was not considered a contraindication if it was not present in the trajectory of the needle or could be dislodged by compression. The shortest possible access for the biopsy was chosen and biopsies of superficially positioned lesions without any parenchymal covering were avoided, if possible. In large lesions, peripheral areas were targeted to avoid central necrosis. When targeting a liver lesion, examiners try to incorporate both surrounding liver tissue as well as the lesion biopsied into the biopsy specimen. All patients considered for intervention met preestablished coagulation parameters as recommended in the European Federation of Societies for Ultrasound in Medicine and Biology guidelines on interventional ultrasound or, if not, received appropriate correction of coagulation parameters.[11] Antiplatelet or antithrombotic medication was discontinued if possible and informed consent for the procedure was obtained prior to the intervention. After proper skin disinfection, local anesthesia (Xylocaine 2%) was administered to the biopsy site. The biopsy needles used in this study included 16 G, 18 G, and 21 G aspiration cutting needles (Sonopsy, Hakko, Nagano, Japan), 18 G Chiba needles for cytology (Bard Angiomed, Karlsruhe, Germany), and 16 G and 18 G semi-automated full core biopsy cutting needles (Biopince™, Argon Medical Devices, Texas, USA). Needle choice was according to the preference of the examiner. Local routine includes an ultrasound control immediately after the intervention as well as 2 h later to rule out any complications and patients are clinically monitored for the next 24 h before being discharged, providing no complications have arisen. As an on-site pathologist was not available at the time of puncture, samples were sent to the department of pathology for further processing.

Figure 1: Biopsy specimen from a liver metastasis; the metastatic tissue is offset as whitish- pink tissue from the surrounding brown liver tissue

Biopsies were performed by physicians working in the ultrasound department with varying levels of experience in ultrasound assisted interventions: Physicians in training with an experience of <100 performed biopsies are supervised by more experienced physicians. More experienced physicians were further divided into two groups with one group containing those with a biopsy history between 101 and 500 biopsies and those with over 501 biopsies in total.

Data collection

Data were collected from both a computerized ultrasound database, recording details of a routine documentation such as the type and size of needle used, location of the lesion, number of passes, lesion size as well as depth of the lesion as measured from the liver surface and the surface of the ultrasound probe and complications resulting from the procedure. In our center, description of whether color transition is present in the biopsy specimen is included in the standardized report and routinely collected, however, the length of the altered tissue is not routinely recorded. Data for gender, body mass index (BMI), experience of the examiner, and pathology results were taken from computerized clinical records.

Two endpoints to evaluate the diagnostic outcome were chosen in the present study: (1) whether any material could be retrieved from the targeted liver lesion, meaning that on microscopic analysis the biopsy specimen showed material different from the surrounding liver parenchyma, even if a definitive diagnosis was not possible and (2) whether a definitive diagnosis could be generated from the lesion biopsy. A "definitive diagnosis" was defined as material retrieved from a biopsy confirming the presence of a liver lesion and leading to a circumscript clinical diagnosis. The diagnostic efficacy of MOSE of liver lesion biopsies was compared to that of other variables, which

have been previously investigated in the context of liver lesion biopsies.

Statistical analysis

Data were analyzed using SPSS version 21.0 (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Distribution of the variables was evaluated by means of the Kolmogorov–Smirnov test. Parametric data are displayed with means and standard deviation, nonparametric data with median and interquartilic range. $P \leq 0.05$ was defined as statistically significant. For univariate analysis *t*-test, Chi-square test or a Mann–Whitney *U*-test was used according to the variable distribution. Both the retrieval of material from the liver lesions and a definitive diagnosis were evaluated as dependent variables. All variables proving to be either significant or to have $P < 0.1$ in the univariate analysis were then subjected to a multivariate analysis (stepwise logistic regression analysis). Institutional review board approval was obtained for the performance of this retrospective cross-sectional study with waiver of informed consent (2017-153). Data are reported following the STrengthening the Reporting of OBservational studies in Epidemiology cross-sectional studies checklist.[12]

Results

Biopsy characteristics, technical data, and complications

All liver lesion biopsies ($n = 264$), including 18 repeat biopsies and 4 biopsies in which absolutely no material could be retrieved, were included in this study [Figure 2 and 3]. The characteristics of the cases are shown in Table 1. Patient gender was balanced and the mean patient age was 64 years, ranging from 15 to 86 years of age. Most patients proved to be slightly overweight with mean BMI being 27.4 kg/m² [Table 1], although only 28 patients (10.6%) had a BMI over 35 kg/m². The mean lesion size was 37.1 mm, encompassing lesions from 5 mm up to 160 mm in diameter, with most lesions being located in the right liver lobe. A number of lesions were located near to the liver surface or the surface of the ultrasound probe, although maximum distance to the liver surface or surface of the ultrasound probe was 73 mm or 100 mm, respectively. The mean number of passes was 1, and in only two cases, more than three passes were performed [Table 1].

A total of ten patients had complications (3.8%) with one major complication (0.4%) (hemobilia), the symptoms of which could be resolved with a stent implantation by means of an endoscopic retrograde cholangiopancreatography intervention,

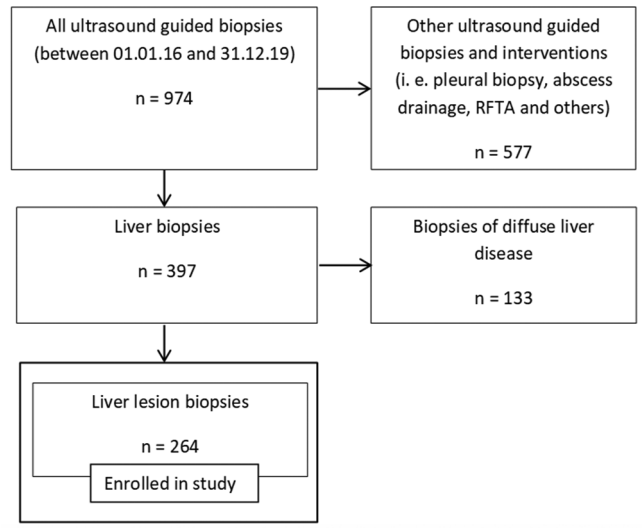

Figure 2: Flowchart of patients included in study

Table 1: Baseline biopsy data; data are displayed either as numbers of cases with percentages or as means and standard deviation as appropriate

Baseline biopsy data	Results
Patient data	
Gender, *n* (%)	
Male	147 (55.7)
Female	117 (44.3)
Average age (years), mean (SD)	64 (13.3)
Average BMI (kg/m²), mean (SD)	27.4 (6.0)
Technical data, *n* (%)	
Needle gauge (G)	
16	146 (55.3)
18	114 (43.2)
21	3 (1.14)
Needle type	
Aspiration cutting needle (Sonopsy)	158 (61.7)
Semi-automated cutting needle (Biopince™)	88 (34.4)
Bard Angiomed Chiba or Sonopsy and Biopince™	10 (3.9)
Lesion data	
Lesion size (mm), mean (SD)	37.1 (29.8)
Location of lesion, *n* (%)	
Right liver lobe	172 (65.2)
Left liver lobe	92 (34.8)
Depth of lesion (mm)	
From liver surface; mean (SD)	20.0 (13.0)
From ultrasound probe; mean (SD)	48.2 (15.2)
Biopsy data, *n* (%)	
Biopsies performed according to experience of examiner (biopsies)	
≤100	51 (19.3)
101-500	61 (23.1)
≥501	152 (57.6)
Number of passes	
1	147 (56.8)
2	86 (33.2)
3	24 (9.3)
>3	2 (1.2)
Sample data	
Fragmentation of sample, *n* (%)	80 (30.8)
Tissue transition present, *n* (%)	96 (36.4)
Length of specimen (mm), mean (SD)	18.0 (9.4)

The total number of cases was 264 except for needle size (n=263), needle type (n=256), number of passes (n=259), and sample data (n=261). The length of the specimen and the fragmentation status are as recorded by the pathologist. The presence or absence of tissue transition was estimated by the examiner. SD: Standard deviation, BMI: Body mass index

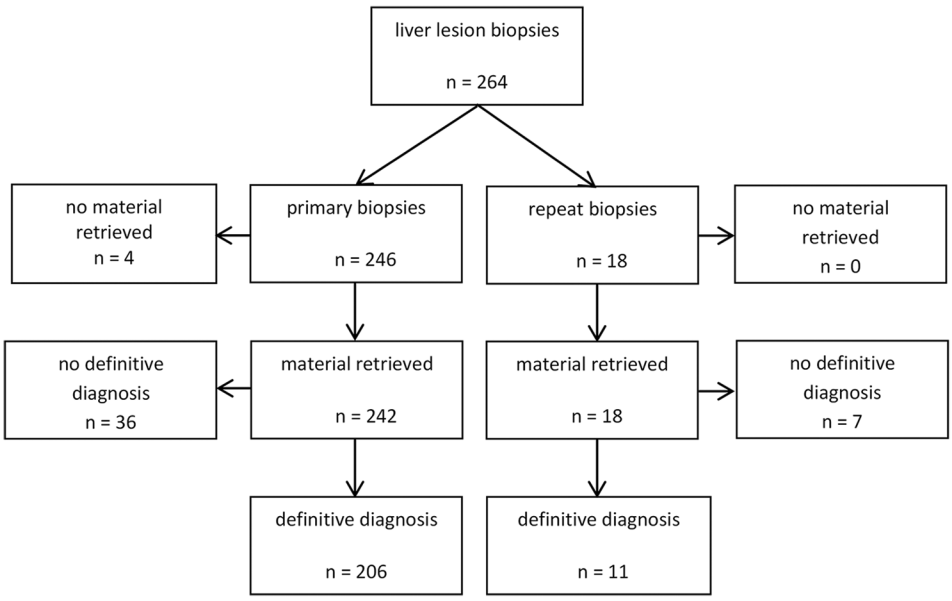

Figure 3: Number of definitive diagnoses and material retrieved from the liver lesion biopsy

and nine minor complications (minor, clinically nonsignificant hemorrhage, and vasovagal reaction).

Biopsy success

Material could be retrieved in a total of 260 of 264 (98.5%) biopsies; material from the targeted lesion could be retrieved in 224 of 264 (84.8%) cases. In total, in 217/264 cases (82.2%), a definitive diagnosis according to definition could be attained [Figure 3]. In four cases, no material for local histological examination was available: in one case, the specimen had been procured in the context of a clinical study for central pathological examination, meaning no further information could be gained. In two other cases, a minor bleeding had occurred immediately after the first biopsy pass without any material being obtained and the examination was terminated. The last case only retrieved very little, highly necrotic material and the patients' clinical situation did not allow any further passes. Histology of the lesions is described in Table 2.

Factors associated to material retrieval and definitive diagnosis

Univariate analysis is shown in Tables 3 and 4. Only the macroscopically visible presence of tissue transition and the type of needle, i.e., either aspiration cutting needle or semi-automated cutting needle as opposed to a combination of both the former needles or the Chiba needle for cytology, were associated to the recovery of material from the lesion and a definitive diagnosis. Gender, BMI, gauge of needle, depth and location of the lesion in the liver, experience of the examiner, number of biopsy passes, and length or fragmentation of the biopsy sample showed $P > 0.1$ on univariate analysis and were not included in the multivariate analysis. A definitive diagnosis was obtained more frequently in those patients who had visible tissue transition (92/96 [95.8%]) as opposed to those who did not (124/165 [75.2%], $P < 0.001$). No difference in outcome could be seen when specifically comparing the outcome of the aspiration cutting to the semi-automated cutting needles. The presence of tissue transition was more common in secondary liver lesions 74/162 (45.7%) as opposed to 18/54 (33.3%) primary liver lesions; however, this difference was not statistically significant ($P = 0.112$). Tissue transition was also

Table 2: Histological results of the lesions biopsied

Histology	Number of patients, *n* (%)
Malignant	
HCC	21 (8)
Bile duct	14 (5.3)
Pancreas	19 (7.2)
Lower gastrointestinal tract	19 (7.2)
Upper gastrointestinal tract	10 (3.8)
Gynecological	32 (12.1)
Pulmonary	14 (5.3)
Hematological	11 (4.2)
Urological	10 (3.8)
Ear/nose/throat	6 (2.3)
Thyroid	1 (0.4)
Skin associated	4 (1.5)
Sarcoma	2 (0.8)
Neuroendocrine	16 (6.1)
Adenocarcinoma (different origin)	12 (4.5)
Undifferentiated	3 (1.1)
Atypical cells	2 (0.8)
Squamous cell	2 (0.8)
Benign	
Benign	19 (7.2)

The total number of cases was 264. Benign lesions included inflammatory lesions, hepatocellular adenoma, regenerative nodules, hemangioma, and extramedullary hematopoiesis. HCC: Hepatocellular carcinoma

Table 3: Univariate analysis of factors influencing the retrieval of material from a liver lesion; only variables presenting as significant or with *P* <0.1 on univariate analysis are presented and were subjected to further multivariate analysis

Variable	Material retrieved from lesion		*P*
	Yes	No	
Patient age (years), mean (SD)	64 (13.8)	66 (10.1)	0.051
Needle type, *n* (%)			
Aspiration cutting	135 (86.0)	22 (14.0)	0.009
Semi-automated cutting	76 (85.4)	13 (14.6)	
Chiba	3 (50.0)	3 (50.0)	
Combination aspiration and semi-automated cutting	1 (33.3)	2 (66.7)	
Lesion size (mm), mean (SD)	38.2 (30.9)	31.2 (23.1)	0.078
Tissue transition present, *n* (%)	93 (96.9)	3 (3.0)	0.000

Variables are shown either as mean value with SD or numbers of cases with percentages as appropriate. The total number of cases was 264 with exception of needle type (*n*=256) and tissue transition present (*n*=261).
SD: Standard deviation

Table 4: Univariate analysis of factors influencing the generation of a definitive diagnosis

Variable	Definitive diagnosis possible		*P*
	Yes	No	
Patient age (years), mean (SD)	64 (13.8)	65 (10.4)	0.072
Needle type, *n* (%)			
Aspiration cutting	133 (84.2)	25 (15.8)	0.001
Semi-automated cutting	75 (84.3)	14 (15.7)	
Chiba	2 (33.3)	4 (66.7)	
Combination aspiration and semi-automated cutting	1 (33.3)	2 (66.7)	
Lesion size (mm), mean (SD)	38.2 (30.9)	31.2 (23.1)	0.078
Tissue transition present, *n* (%)	92 (95.8)	4 (4.2)	0.000

Variables are shown either as mean value with SD or numbers of cases with percentages as appropriate. Only variables presenting as significant or with *P*<0.1 on univariate analysis are presented and were subjected to further multivariate analysis. The total number of cases was 264 with exception of needle type (*n*=256) and tissue transition present (*n*=261).
SD: Standard deviation

present in benign lesions 6/19 (31.6%), although less common than in malignant lesions 86/198 (43.4%).

In the multivariate analysis, only the presence of tissue transition in the biopsy specimen and the type of needle, i.e., either the aspiration cutting or the semi-automated cutting biopsy needle as opposed to a combination of both or the Chiba needle, were independent predictors for obtaining a definitive diagnosis. For retrieving material from a liver lesion, only the presence of tissue transition in the biopsy specimen and the type of needle used were identified as independent predictors [Table 5].

Discussion

This study shows that the presence of macroscopically visible tissue transition as shown by MOSE is an independent predictor of a successful liver biopsy together with the type of the needle used. Although in the context of liver lesion biopsies this phenomenon is probably well known to experienced examiners, so far it has not been reported as a tool which can be used to guide a liver lesion biopsy. MOSE of conventional endoscopic-ultrasound-assisted fine-needle aspiration biopsies has recently been evaluated in a randomized controlled trial and has shown to achieve a similar diagnostic yield but with fewer passes compared to the conventional endosonographic technique.[10] This method is easily performed and is readily available in clinical practice, especially if no on-site pathologist is present to confirm the presence of material other than liver tissue. To observe the presence of a color transition in the biopsy specimen, surrounding liver tissue as well as tissue from the lesion has to be obtained. In the present study, observation of tissue transition tended to be more frequent in metastatic lesions than in lesions originating primarily from the liver, which might be less likely to show overt differences in tissue color due to their similarities with the normal liver parenchyma.

It may seem that the present study has a lower success rate (84.8%/82.2%) than some previous studies (over 90%), although some studies have described even lower rates between 61% and 80%.[5,6,9,13-17] The differences between the studies depend enormously on the study population and the definition used for a successful biopsy. Indeed, some studies with high success rates included only biopsies of metastases, excluding benign or primary neoplasm of the liver.[13] Lower success rates were obtained when all liver lesion biopsies were included and a strict definition of success was applied,[9] as is the case in our study. In the present study, the definition of success was based on the definite histological diagnosis. Diagnoses which were compatible with, but not definite, were not considered as successful. This is more strict than regular clinical practice, since the clinician integrates information from different sources to achieve a definite diagnosis in a patient. Previous studies have described a generally lower diagnostic sensitivity for hepatocellular carcinoma (HCC) compared to metastatic lesions.[1,17] This could have also influenced the present results, as HCC was the second most common diagnosis in this study.

In this study, the independent influence of different factors which could affect the outcome of the diagnostic procedure was comprehensively evaluated, with comparable results to previous studies.[1,5,8] Interestingly, on multivariate analysis, the only other factor besides tissue transition was the use of more than one type of needle, which reflects the perceived difficulty of the biopsy.

There were several limitations to our study. First, due to its retrospective design, the study relies on the accuracy and completeness of the documentation of data and the estimation of each individual examiner. Description of whether visible tissue transition is present is routinely collected in the

Table 5: Multivariate analysis of factors influencing the retrieval of material from a liver lesion and attainment of a definitive diagnosis

Variables introduced	Final model	OR	95% CI	*P*
Retrieval of material from a liver lesion				
Age, tissue transition present, needle type, lesion size (ungrouped)	Tissue transition present	9.174	2.703-31.141	0.000
	Needle type	0.235	0.059-0.938	0.040
	Lesion size	1.014	0.998-1.030	0.091
Generation of a definitive diagnosis				
Age, tissue transition present, needle type, lesion size (ungrouped)	Tissue transition present	7.527	2.561-22.124	0.000
	Needle type	0.163	0.038-0.690	0.011
	Lesion size	1.013	0.998-1.028	0.071

OR: Odds ratio, CI: Confidence interval

standardized digital report program, but not the length of the changes. Secondly, color transition might not have been present in biopsies in which only tissue from the liver lesion and no surrounding liver tissue had been obtained. Although the evaluation of color transition is easily performed in metastatic lesions, which might show more overt differences, estimation of color transition in tumors originating primarily in the liver might be more difficult and examiner dependent. Finally, another possible limitation of this study might also be the strict definition of a reaching a definitive diagnosis by histology only, as a clinical diagnosis usually is achieved by combining results from different diagnostic sources.

Conclusion

The presence of tissue transition as observed by MOSE of liver lesion biopsy samples can predict their successful outcome. Macroscopic evaluation of tissue transition can easily be applied in a clinical setting when performing liver lesion biopsies to evaluate the adequacy of the specimen obtained.

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Conflicts of interest

There are no conflicts of interest.

References

1. Howlett DC, Drinkwater KJ, Lawrence D, Barter S, Nicholson T. Findings of the UK national audit evaluating image-guided or image-assisted liver biopsy. Part I. Procedural aspects, diagnostic adequacy, and accuracy. Radiology 2012;265:819-31.
2. Colloredo G, Guido M, Sonzogni A, Leandro G. Impact of liver biopsy size on histological evaluation of chronic viral hepatitis: The smaller the sample, the milder the disease. J Hepatol 2003;39:239-44.
3. Westheim BH, Aagenæs I, Østensen AB, Sanengen T, Almaas R. Effect of operator experience and frequency of procedure performance on complication rate after ultrasound-guided percutaneous liver biopsies. J Pediatr Gastroenterol Nutr 2013;57:638-43.
4. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver biopsy. Hepatology 2009;49:1017-44.
5. Appelbaum L, Kane RA, Kruskal JB, Romero J, Sosna J. Focal hepatic lesions: US-guided biopsy – Lessons from review of cytologic and pathologic examination results. Radiology 2009;250:453-8.
6. Yu SC, Lau WY, Leung WT, Liew CT, Leung NW, Metreweli C. Percutaneous biopsy of small hepatic lesions using an 18 gauge automated needle. Br J Radiol 1998;71:621-4.
7. Solmi L, Muratori R, Brambati M, Gandolfi L. Comparison between the 21-gauge Urocut needle and the 21-gauge Surecut needle in echo-guided percutaneous biopsy of neoplastic liver lesions. Surg Endosc 1989;3:38-41.
8. Kim JS, Won HJ, Lee SJ, Kim SY, Shin YM, Kim PN. Utility and safety of repeated ultrasound-guided core needle biopsy of focal liver masses. J Ultrasound Med 2018;37:447-52.
9. Knöpfle E, Bohndorf K, Wagner T. Does the core biopsy of solid liver lesions permit an exact histological classification? Results of a prospective study under routine clinical conditions. Rofo 1997;167:406-11.
10. Iwashita T, Yasuda I, Mukai T, Doi S, Nakashima M, Uemura S, *et al.* Macroscopic on-site quality evaluation of biopsy specimens to improve the diagnostic accuracy during EUS-guided FNA using a 19-gauge needle for solid lesions: A single-center prospective pilot study (MOSE study). Gastrointest Endosc 2015;81:177-85.
11. Sidhu PS, Brabrand K, Cantisani V, Correas JM, Cui XW, D'Onofrio M, *et al.* EFSUMB Guidelines on Interventional Ultrasound (INVUS), Part II. Diagnostic ultrasound-guided interventional procedures (Short Version). Ultraschall Med 2015;36:566-80.
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. Lancet 2007;370:1453-7.
13. Elsayes KM, Ellis JH, Elkhouly T, Ream JM, Bowerson M, Khan A, *et al.* Diagnostic yield of percutaneous image-guided tissue biopsy of focal hepatic lesions in cancer patients: Ten percent are not metastases from the primary malignancy. Cancer 2011;117:4041-8.
14. Buscarini L, Fornari F, Bolondi L, Colombo P, Livraghi T, Magnolfi F, *et al.* Ultrasound-guided fine-needle biopsy of focal liver lesions: Techniques, diagnostic accuracy and complications. A retrospective study on 2091 biopsies. J Hepatol 1990;11:344-8.
15. Schmidt AJ, Kee ST, Sze DY, Daniel BL, Razavi MK, Semba CP, *et al.* Diagnostic yield of MR-guided liver biopsies compared with CT- and US-guided liver biopsies. J Vasc Interv Radiol 1999;10:1323-9.
16. Dusenbery D, Ferris JV, Thaete FL, Carr BI. Percutaneous ultrasound-guided needle biopsy of hepatic mass lesions using a cytohistologic approach. Comparison of two needle types. Am J Clin Pathol 1995;104:583-7.
17. Fornari F, Filice C, Rapaccini GL, Caturelli E, Cavanna L, Civardi G, *et al.* Small (< or=3 cm) hepatic lesions. Results of sonographically guided fine-needle biopsy in 385 patients. Dig Dis Sci 1994;39:2267-75.