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Ultrasound-guided tru-cut biopsy of abdominal and pelvic tumors in gynecology

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KEYWORDS: advanced abdominal tumor; pelvic tumor; tru-cut biopsy; ultrasound diagnosis

ABSTRACT

Objective *To analyze the safety, adequacy and accuracy of tru-cut biopsy and to evaluate factors potentially affecting adequacy.*

Methods *We analyzed retrospectively a group of patients who had undergone tru-cut biopsy for either primary suboptimally operable tumors, recurrence or suspected non-genital or secondary tumor. Tru-cut biopsy was performed either transvaginally or transabdominally, using an automatic biopsy gun with disposable needle and needle guide attached to the probe. The adequacy, i.e. obtaining a sample sufficient for identification of the origin of the tumor and performance of immunohistochemistry; accuracy, i.e. agreement between biopsy and final postoperative histology; and safety, as determined by complication rate, were assessed. Variables potentially influencing adequacy were analyzed using the orthogonal projections to latent structure method.*

Results *A total of 195 biopsies were performed on 190 patients. An adequate sample was obtained in 178 (91.3%) biopsies. The final histology was not in agreement with the result from tru-cut biopsy in two out of 118 patients who underwent subsequent surgery (accuracy 98.3%). There were complications in two cases out of the 195 biopsies performed (1.0%). Ascites, elevated CA 125, primary suboptimal operable tumor, serous epithelial ovarian cancer histology, carcinomatosis and vaginal approach were significant positive predictors for the achievement of an adequate sample, while recurrence as an indication, non-serous and non-ovarian histotypes and transabdominal approach were negative predictors.*

Conclusion *Ultrasound-guided tru-cut biopsy is an efficient, minimally invasive, accurate and safe diagnostic method in the management of advanced, recurrent or atypical abdominal and pelvic tumors of probable non-genital origin, where unnecessary laparotomy or laparoscopy can be avoided. The adequacy of tru-cut biopsy is mainly influenced by indication group, histology, site of biopsy and approach. Our analysis can help in counseling the patient before the procedure and helps to explain the possible causes of failure of the procedure. Copyright © 2010 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

The currently available minimally invasive techniques for obtaining tissue samples, especially in patients where there are doubts concerning the benefit of a primary surgical intervention or the nature of the lesion (uncertain recurrence of the tumor, suspected tumor metastasis or cases of advanced tumors of probably non-genital origin), include fine-needle aspiration biopsy and tru-cut biopsy[1]. The frequently used aspiration biopsy is a simple technique, but the amount and integrity of collected tissue are limited, leading to cytological rather than histological evaluation[2].

Tru-cut biopsy, on the other hand, provides a sample with preserved tissue architecture, allowing comprehensive histological evaluation including immunohistochemistry[3]. Studies published so far deal almost exclusively with tru-cut biopsy of abdominal and pelvic tumors under computed tomography (CT) control[4,5]. In these studies, cutting (tru-cut) and fine-needle biopsies were found to be comparable in obtaining adequate material, but the cutting needle provides a superior specificity of diagnosis. Only one study – from our center – has presented experience with tru-cut biopsy under ultrasound control in the management of abdominal and pelvic tumors. In that study a high

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diagnostic accuracy with a minimum of complications was achieved[3].

Nonetheless, data describing factors affecting the accuracy of tru-cut biopsy under ultrasound control are not available. The aim of the present work was to determine the adequacy, safety and accuracy of tru-cut biopsy performed under ultrasound guidance on a large group of patients and assess factors that may affect adequacy.

METHODS

Indications for tru-cut biopsy

Data from patients who had undergone tru-cut biopsy at the Oncogynecological Centre of the General Teaching Hospital in Prague between 2005 and 2009 were included. The ultrasound-guided tru-cut biopsy technique was used for the purposes of tissue sampling and tumor verification prior to treatment planning. The referred patients had advanced abdominal and pelvic tumors and would not benefit from primary oncogynecological surgery, or the origin of the tumor was unclear and further management required histological verification.

The following indication groups were identified: Group A ($n = 104$), inoperable tumors (cases with abdominal and pelvic tumors with parameters of primary suboptimal operability); Group B ($n = 31$), suspicion of metastases to the ovaries or peritoneum (cases with history of non-gynecological tumor and current signs of secondary ovarian or peritoneal tumor); Group C ($n = 27$), recurrence (cases with a history of gynecological tumor and current uncertain signs of recurrence); Group D ($n = 25$), non-genital tumors (tumors with an atypical imaging morphology, considered to be of non-genital origin); and Group E ($n = 3$), other (including three rare indications – two cervical tumors not accessible vaginally and one tumor in a hysterotomy scar) (Table 1).

Suitability for optimal cytoreduction was evaluated by ultrasound in combination with CT or magnetic resonance imaging (MRI). The following findings were considered as signs of primary optimal inoperability: either multiple or non-resectable metastases in parenchymatous organs, extensive small bowel involvement (such as diffuse visceral carcinomatosis), bulky mesenterial disease, bulky suprarenal lymph nodes or extra-abdominal non-resectable disease.

Table 1 Characteristics of the study group with respect to indication

Indication for tru-cut biopsy	n *(%)*
Group A (inoperable tumors)	104 (54.7)
Group B (suspected metastasis)	31 (16.3)
Group C (recurrence)	27 (14.2)
Group D (non-genital tumors)	25 (13.2)
Group E (other)	3 (1.6)
Total	190 (100.0)

In cases where metastatic disease was suspected (Group B), tru-cut biopsy was indicated in patients with advanced disease. Patients with signs of recurrent gynecological tumors were referred for biopsy if the diagnosis was uncertain on the basis of imaging methods, clinical examination and tumor markers. Advanced tumors with an atypical imaging morphology (i.e. a larger part of the tumor mass above the pelvis, dominant lymphadenopathy with minimal findings on the ovaries or the peritoneum, irregular, yet non-necrotic structure of the solid part of the tumor, etc.) were assessed as probable primary non-genital malignancies.

All patients with poor performance status who were not suitable for open surgery or laparoscopy (this could be an independent indication for tru-cut biopsy) suffered from inoperable tumors and were therefore included in the group of cases with unachievable optimal cytoreduction. Written informed consent approved by the local ethics committee was obtained from each patient prior to the procedure.

Analysis of adequacy, accuracy and safety

Only samples allowing identification of tumor origin and sufficient histological evaluation including immunohistochemistry were considered adequate. Several variables were tested as potential factors influencing adequacy of tru-cut biopsy: age, body mass index (BMI), CA 125 level, indication group, operator, histology, biopsy site, biopsy approach and ascites. Accuracy was assessed as agreement between tru-cut biopsy histology and final operational histology in patients who underwent surgery and safety was assessed as the rate of severe complications in the group.

Ultrasound-guided tru-cut biopsy technique

Biopsies were performed by two experienced operators and one trainee using the Fast-gun automatic biopsy system (Sterylab, Milan, Italy) and 18-G/25 cm core-cut biopsy needle. An ultrasound machine with endovaginal (5–7.5-MHz) and transabdominal (3–5-MHz) probes (Mindray, Shenzhen, China) was used. No anesthesia was needed for vaginal biopsy; local anesthesia by infiltration of the abdominal wall with 10 mL of 1% trimecain was used for transabdominal biopsy. In the transvaginal approach a special needle guide (Jezek, Prague, Czech Republic), similar to that used for oocyte retrieval, was attached to the vaginal ultrasound probe. The transabdominal biopsy was performed with the free hand controlling the needle tip by positioning the transabdominal ultrasound probe in a manner similar to that used for amniocentesis. The tip of the biopsy needle was carefully visualized during the whole procedure to achieve optimal sampling and patient safety. At the end of the biopsy procedure, bleeding from the biopsy site and vaginal bleeding were checked.

The biopsy was made from different sites of primary, advanced, recurrent or metastatic tumor: the ovarian or recurrent tumor itself, parietal or visceral carcinomatosis,

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omental cake, pelvic lymph nodes or other rare sites (cervical tumors and scar after uterotomy). The technique can be seen on a videopresentation on the website of the European Society of Gynaecological Oncology[6]. One to three tissue cylinders 10–20 mm long (depending on the size of the biopsied lesion) were obtained from each patient. All the material obtained from each patient was fixed in formalin, and slides from paraffin-embedded tissue blocks were stained with hematoxylin and eosin. Each sample was examined for the presence of tumor, sufficiency of tissue and suitability for immunohistochemistry staining. If a tumor was present, its origin, type and grade (if applicable) were assessed, and immunohistochemistry for typing was performed in each adequate sample. Patients were observed for 120 min following the biopsy and then discharged. No antibiotic therapy was administered.

Statistical analysis

To eliminate skewed data distribution and heteroscedasticity, the original data were transformed to a Gaussian distribution before being further processed by a power or logarithmic transformation using Statgraphics Centurion statistical software, version XV (Statpoint Inc., Herndon, VA, USA). The transformed data underwent multivariate regression using the method of orthogonal projections to latent structure (OPLS), which is a modification of the method of partial least squares multivariate regression (PLS). Both methods are effective in coping with the problem of severe multicollinearity within the matrix of independent variables[7].

PLS, instead of using the original explanatory variables directly, constructs a new set of regressor variables as linear combinations of the original variables. The linear combinations are chosen sequentially in such a way that each new regressor has maximal sample covariance with the response variable, subject to being uncorrelated with all previously constructed regressors[8]. In contrast to PLS, OPLS is able to separate the variability in the matrix of independent variables that is shared with the vector of the dependent variable from the variability that is shared within the matrix of independent variables[7].

In our model, the single dependent variable was the adequacy of the histological sample from the tru-cut biopsy, while the other factors (age, BMI, CA 125 level, indication, operator, histology, biopsy site, biopsy approach, ascites) represented the independent variables. OPLS enabled us to find the best predictors as well as the best combination of predictors of adequacy of the histological sample achieved by tru-cut biopsy.

RESULTS

Group characteristics

A total of 195 biopsies were performed on 190 patients (with five repeat biopsies in five patients). The median patient age was 63 (range, 22–92; SD 12.94) years and median BMI was 25.9 (range, 14.8–48.7; SD 5.87) kg/m^2. Biopsy parameters (site, approach and histology) are summarized in Table 2.

Table 2 Characteristics of the study group with respect to biopsy site, approach and histology, with corresponding adequacy for each variable

Parameter	n *(%)*	*Corresponding adequacy* (n *(%)*)
Site of biopsy		
Tumor	125 (64.1)	118 (94.4)
Carcinomatosis	41 (21.0)	41 (100.0)
Omental cake	12 (6.2)	11 (91.7)
Lymph node	11 (5.6)	10 (90.9)
Other	6 (3.1)	3 (50.0)
Total	195 (100.0)	178 (91.3)
Approach		
Transvaginal	131 (67.2)	124 (94.7)
Transabdominal	64 (32.8)	59 (92.2)
Histology		
SOC	77 (39.5)	76 (98.7)
OOC	20 (10.3)	19 (95.0)
Non-ovarian histology		
Malignant	83 (42.6)	76 (91.6)
Benign	10 (5.1)	7 (70.0)

OOC, histotypes of epithelial ovarian cancer other than SOC; SOC, serous ovarian cancer.

Adequacy

An adequate sample was obtained in 178 of 190 (93.7%) cases, corresponding to 178 of 195 (91.3%) biopsies. In 17 patients the material obtained by primary biopsy was evaluated as inadequate for identification of the tumor origin. In five of these patients the biopsy was repeated and an adequate sample obtained. Six patients (3.2%) with inadequate sample underwent laparotomy or laparoscopy for the assessment of histological diagnosis. Another six patients of poor performance status with advanced disease, in whom the first biopsy was inadequate, died before the completion of the investigation.

The results of the OPLS multivariate regression analysis of potential factors influencing the adequacy of tru-cut biopsy are shown in Table 3. Age and BMI did not influence the adequacy of the biopsy sample. Ascites and elevated CA 125 levels were positive predictors for the achievement of an adequate sample. Among indications, significantly better adequacy was present in the group of patients referred for primary inoperable tumor, while a significant negative correlation presented in those with uncertain signs of recurrence.

With respect to final histology, serous epithelial ovarian cancer histology correlated positively with adequacy; other ovarian cancer histotypes did not influence adequacy significantly, while all other non-ovarian tumors were the strongest negative predictors of sample adequacy. The specific adequacy for each histotype is summarized in Table 2. Biopsies taken from carcinomatosis (both parietal and visceral) provided

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Table 3 Dependency of adequacy on selected parameters as evaluated using multivariate regression (orthogonal projection to latent structures)

Variable	*Parameter (component loading)*	*1.96 × SE*	*Parameter/ 1.96 × SE*	P	*Correlation with common predictive component*	*Influence on adequacy*
Dependent variable						
Adequacy	1.000	0.217	4.614	< 0.01	0.370	—
Predictors						
Patient characteristics						
Age	0.142	0.197	0.720	NS	0.232	None
BMI	−0.001	0.165	−0.006	NS	−0.003	None
Ascites	0.328	0.152	2.152	< 0.01	0.538	Positive
CA 125	0.395	0.076	5.203	< 0.01	0.658	Positive
Reasons for biopsy						
Inoperable tumor	0.361	0.134	2.695	< 0.01	0.592	Positive
Suspected metastasis	−0.088	0.195	−0.450	NS	−0.146	None
Recurrence	−0.224	0.219	−1.021	< 0.05	−0.365	Negative
Atypical morphology	−0.165	0.128	−1.295	< 0.05	−0.272	Negative
Other indication	−0.095	0.204	−0.467	NS	−0.154	None
Operator						
Operator 1	−0.029	0.108	−0.273	NS	−0.049	None
Operator 2	0.190	0.178	1.069	< 0.05*	0.312	?
Operator 3	−0.106	0.121	−0.872	NS	−0.173	None
Histology						
SOC	0.473	0.128	3.701	< 0.01	0.779	Positive
OOC	0.087	0.108	0.801	NS	0.142	None
Non-ovarian	−0.503	0.079	−6.385	< 0.01	−0.829	Negative
Biopsy site						
Tumor	−0.035	0.169	−0.208	NS	−0.060	None
Carcinomatosis	0.231	0.117	1.969	< 0.01	0.380	Positive
Omentum	0.024	0.138	0.171	NS	0.037	None
Lymph node	−0.108	0.173	−0.621	NS	−0.175	None
Other site	−0.193	0.240	−0.806	NS	−0.315	None
Biopsy approach						
Vaginal	0.230	0.195	1.180	< 0.05	0.376	Positive
Abdominal	−0.230	0.195	−1.180	< 0.05	−0.376	Negative
R^2a			0.137			
Q^2b			0.051			

aR^2 is the proportion of variation of the dependent variable explained by the model. *b*Q^2 is the proportion of variation of the dependent variable predicted by the model according to cross validation. Parameter/1.96 × SE gives an indication of the statistical certainty of the influence of each variable on adequacy. *Value of borderline statistical significance. BMI, body mass index; NS, not significant; OOC, histotypes of epithelial ovarian cancer other than SOC; SOC, serous ovarian cancer.

significantly better results than did those from other locations (tumor, omental cake, lymph node). The transvaginal biopsy approach correlated positively with adequacy, while the transabdominal approach correlated negatively.

Accuracy

In 118 patients with adequate samples from tru-cut biopsy, an interval debulking surgery (residual disease was present in all these patients) or primary surgery (e.g. for recurrent disease, suspected metastasis, non-genital tumors) was performed as part of their further management. The final histology was not in agreement with the result from tru-cut biopsy in only two cases out of these 118 patients (1.7%). In the first case, the histology from the tru-cut biopsy showed leiomyoma while the final report after the surgery confirmed low-grade leiomyosarcoma. In leiomyosarcomas, especially in tumors with lower proliferation activity, the distinction of a sarcoma from a benign myoma in a smaller tissue sample – especially if taken from the periphery of the tumor – is very difficult. In the second case, the histology from the biopsy revealed mucinous adenocarcinoma with probable origin in the reproductive organs. The final histology showed the origin of this tumor in the colon. The differentiation between a genital and intestinal origin of such tumors is very difficult even if immunohistochemistry is performed.

Safety

There were complications following the procedure in two cases out of the 195 biopsies performed (1.0%). In both of the patients with complications, bleeding after tru-cut biopsy required surgery. In the first case, laparotomy was performed due to hemoperitoneum and revealed bleeding from the biopsy site on the surface

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of the secondary ovarian tumor (Krukenberg tumor) with rich vascularization. Adnexectomy was performed to control the bleeding. This patient suffered from thrombocytopenia as a consequence of bone marrow infiltration by an advanced disseminated tumor. We currently consider thrombocytopenia to be a significant contraindication for tru-cut biopsy. In the second patient, ultrasound examination revealed bleeding into the ascitic fluid from the site of the biopsy of pelvic carcinomatosis. A laparoscopy was performed immediately, but in the meantime the bleeding stopped spontaneously. Similar signs of transitory bleeding into the ascitic fluid, which ceased shortly once the intervention had been completed, were evident on ultrasound in three other patients. All of these patients, however, were clinically stable and their postoperative state did not require surgery or any other therapeutic intervention.

DISCUSSION

This paper describes a 5-year experience in performing tru-cut biopsies. The high reliability and safety of this minimally invasive method have been confirmed in a large cohort of patients. We demonstrated high adequacy (178 of 195 biopsies (91.3%)), accuracy (agreement with final surgical histology in 98.3% of patients operated on) and safety (complication rate of 1.0%). The positive predictors of adequate sample retrieval were presence of ascites, high CA 125 level, indication of suboptimally operable tumor and serous ovarian cancer, while the negative predictors were indication of suspicious recurrence or atypical morphology and non-ovarian histology.

In a considerable proportion of the patients (25–29%) with advanced abdominal and pelvic tumors or patients with uncertain origin of the tumor the management of the disease did not require primary surgery[9]. However, histological verification of the origin of the tumor is an essential prerequisite for further management.

At present the most frequent minimally invasive biopsy technique is fine-needle aspiration biopsy (FNAB). A thin needle of 19–22-G (≤ 0.9 mm) is used to obtain tissue by aspiration. First described in 1921, this has been for many years the standard method for histological verification of tumors in various locations. The main limitations of this method, however, are the small sample size and often disrupted tissue architecture, resulting in a high rate of inadequate samples for histological assessment. Moreover, limited sample quality may not allow immunohistochemistry staining, which could play a crucial role in the differential diagnosis, especially of colon and ovarian cancer.

Several papers have compared FNAB and tru-cut biopsy. The largest study – of 1300 consecutive CT-guided biopsies from chest, abdomen, retroperitoneum and head/neck regions – evaluated the adequacy and specific diagnosis rates of FNAB (22-G needle) and tru-cut biopsy (16–18-G needle)[4]. Adequate samples were obtained in 72–92% of cases using FNAB and 93–100% using tru-cut biopsy; the specific diagnosis rates were 54–67% and 82–100%, respectively. Bdour *et al.*[5] compared FNAB and tru-cut biopsy in the sampling of breast lesions and reported a sensitivity of 97% using tru-cut biopsy compared with 90% for FNAB. In addition, immunohistochemistry could be performed in all tru-cut biopsy samples.

In an earlier paper we described our initial experience with tru-cut biopsy in patients with advanced pelvic tumor[3]. The current analysis of a cohort of twice the size allows for the analysis of factors that may affect adequacy. A higher adequacy of transvaginal biopsies is probably due to the proximity of the biopsy lesion to the probe and a better capacity for guiding the biopsy probe more precisely into the vascularized, i.e. vital, parts of the tumor. CA 125 levels and the presence of ascites correlated positively with adequacy. This can easily be explained by the large tumor load in these cases. A larger tumor is easier to access (especially if accessible transvaginally). Carcinomatosis, as a biopsy site that is often easily accessible transvaginally in the pouch of Douglas and transabdominally by a peritoneal approach through the anterior abdominal wall, also correlated positively with adequacy. Besides its presence close to the biopsy site, rich vascularization can often be identified in these nodules by power Doppler ultrasonography to help direct the biopsy. The serous histotype of ovarian cancer was a strong positive predictor of adequacy. This histotype is often present as solid nodules of carcinomatosis and a large tumor load in advanced inoperable cases. Non-ovarian tumors were, on the other hand, a strong negative predictor. This finding cannot be easily explained.

Inoperable/suboptimally operable tumor was a favorable indication with a strong positive correlation with adequacy. This finding is in concordance with the above-mentioned explanation. A large tumor mass as a biopsy site is usually accessible in these patients, while in patients with recurrent tumor or with tumor of atypical morphology only small, necrotic or cystic lesions are often present.

One of the operators achieved slightly better results in adequacy. Surprisingly, she was a trainee; the explanation probably lies in the fact that she tended to perform biopsies in less difficult cases (performing only 16% of all biopsies).

Although obesity is considered a factor impeding the accuracy of ultrasound – thus also potentially affecting the performance of tru-cut biopsy (especially by the abdominal approach) – BMI did not affect adequacy in our study. One of the explanations could be a tendency towards a transvaginal approach in obese patients, but this was not confirmed and the proportion of transabdominal and transvaginal biopsies was the same in the non-obese (BMI < 30) and obese (BMI > 30) sub-groups. Another plausible reason could be the higher tumor load due to later diagnosis in obese patients. However, a higher proportion of cases with neither high CA 125 nor ascites was found among obese patients in our study. Thus, equal adequacy of tru-cut biopsy in non-obese and obese

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patients remains an unexpected finding for which we cannot offer a satisfactory explanation.

One of the important parameters in the assessment of tru-cut biopsy is accuracy, i.e. conformity between the histological diagnosis made from the biopsy and the final histology of the tumor achieved by surgery. In our cohort discordance was found in only two cases.

Several modalities can be used to guide tru-cut biopsy including ultrasound, CT, MRI and a digitally directed approach. CT-guided percutaneous biopsy has been established as an efficient and safe procedure in the evaluation of retroperitoneal and abdominal masses, but it has certain limitations in the case of deep pelvic masses due to limited transabdominal accessibility or limited imaging in the osseous pelvic space. MRI is used only rarely, despite its imaging benefits, as it requires special non-magnetic equipment and experience[10].

Ultrasound guidance benefits mainly from its availability. It offers high flexibility in the choice of biopsy approach (transabdominal, transvaginal, transrectal) and short procedure time. The absence of radiation is an additional benefit compared with CT-guidance. Ultrasound-guided tru-cut biopsy also allows precise real-time acquisition of tissue with whole-procedure control of the needle tip. In combination with color Doppler imaging it also facilitates the choice of a vital part of the tumor for biopsy. Precise guidance of the needle tip during the whole procedure also eliminates the risk of bleeding complications. In our study we witnessed these complications in a proportion comparable to that experienced with FNAB[11].

In conclusion, this study demonstrates that ultrasound-guided tru-cut biopsy is an efficient, minimally invasive, accurate and safe diagnostic method in the management of advanced, recurrent or atypical abdominopelvic tumors of likely non-genital origin where unnecessary laparotomy or laparoscopy can be avoided. The adequacy of tru-cut biopsy is mainly influenced by indication group, expected histology, site of biopsy and approach. This analysis can help in counseling the patient before the procedure and helps to explain the possible causes in cases of failure of the procedure.

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