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INTERVENTIONAL

Ex vivo performance comparison of three percutaneous biopsy needle systems

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Abstract

Purpose The aim of this study is to identify the micro-mechanical characteristics that define biopsy performance in normal ex vivo animal organs.

Materials and methods Three biopsy systems with differences of needle external diameter, tray height and effective tray length were assessed. Sampling was performed in porcine liver and kidneys with commercially labelled 14G, 16G and 18G, using 2-cm throw needle systems. Five samples were obtained per needle size and per organ, and the experiment was repeated twice for a total of 90 biopsy cores. Samples were analysed and compared in terms of macroscopic aspect, sample length, weight and tissue architecture.

Results The system with the longest effective needle tray (system A) has shown significant superiority ($p < 0.001$) versus the other systems regarding the mean weight of tissue obtained for all needle sizes. Furthermore, the 14G needle of system A has shown superiority regarding the number of portal spaces and the 16G regarding the length of kidney fragments obtained.

Conclusion The outcomes obtained with the different biopsy systems were not equal. The micro-mechanical characteristic that appears to influence the quantity and quality of the obtained tissue is the effective needle tray length and not the needle external diameter or the needle tray height. This information should be taken into account in the future design of biopsy needle systems, particularly when potentially used in the assessment of biomarkers and the characterisation of tumour micro-environment.

Key Points

- *The amount of obtained tissue mass is not the same among percutaneous biopsy needle systems.*
- *There are different micro-mechanical characteristics that condition the amount of obtained tissue.*
- *The micro-mechanical characteristic that offers more tissue mass for the same calibre is the effective length of the needle tray.*

Keywords Biopsy · Liver · Kidney · Tissue

Abbreviations

ANOVA	Analysis of variance
DNA	Deoxyribonucleic acid
FNA	Fine needle aspiration
G	Gauge
SD	Standard deviation
SPSS	Statistical Package for the Social Sciences
UK	United Kingdom
USA	United States of America

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Introduction

Percutaneous biopsies are of paramount importance for the management of oncologic patients. Biopsies have been traditionally used for tissue characterisation; therefore, minimal change has occurred in the last two or three decades on the design of biopsy systems [1]. As percutaneous biopsies are more integrated to precision medicine and in particular to biomarkers assessment, tumour micro-environment and tumour heterogeneity characterisation, the standards of

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percutaneous biopsies, are changing [2]. Repeating biopsies lead to frustration, treatment delay and exclusion from research trials; therefore, there is increased pressure for sample adequacy extending further from histological diagnosis.

In clinical practice, some systems appear to perform better than others in terms of tissue quantity and quality. This performance discrepancy between needle systems is attributed to the micro-mechanical design of each device. The characteristics that define the quality of the sample have not been analysed, and the use of needles is merely empirical.

The purpose of this in vitro study is to assess the performance of three popular biopsy systems and define the needle micro-mechanical characteristics that influence the quantity and the quality of the obtained sample.

Materials and methods

Study hypothesis

The hypothesis of this in vitro study is that there is a significant difference in terms of tissue mass and tissue quality among commercially available percutaneous biopsy needle systems of the same external calibre.

Study design and methods

Three popular commercially available systems were tested in the study: system A (Achieve, Becton Dickinson), system B (Magnum, Bard Biopsy Systems) and system C (Temno Evolution, Becton Dickinson). The three needle systems were tested for the three following calibre sizes: 14, 16 and 18G according to the most common use in clinical practice. A 2-cm throw was used for all the three systems.

The needles differed in the following characteristics: (a) needle external diameter, (b) needle tray height and (c) needle tray length. The technical characteristics of the three needle systems are shown in Fig. 1 and in Table 1. The needles were tested in porcine liver and porcine kidneys due to the similarities with human tissue. Organs were treated according to ethical rules and legislation, and local approval for the experiment was obtained. The animal organs were obtained from an abattoir controlled by an official veterinarian. Organs were removed, within 1 h after slaughtering, from healthy female pigs (race, Edelschwein; age, about 5 months), kept on ice and transferred to the laboratory.

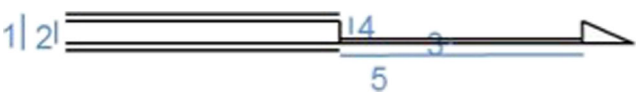

Fig. 1 Needle micro-mechanical characteristics. 1: needle external diameter, 4: needle tray height (comes from the extraction of 2–3) and 5: effective needle tray length

In order to obtain statistically significant results, five biopsy cores per organ and per needle were taken, within 6 h after obtaining the organs. The experiment was repeated two times for a total of 90 biopsies for organ. The experiment took place on two different sessions with the presence of an interventional radiologists and a laboratory technician. Specimens were put on a piece of bench liner "Bench Guard" (Sterilin Ltd.) and weighed using a GEM20 digital jewellery scale (Smart Weigh) before being stored in 10% phosphate buffered formalin solution (approx. 4% formaldehyde, pH 7.2).

Samples were stored at a room temperature and were transferred to the pathologist within 3 days of fixation. Pathology analysis with a scoring system on the basis of the following parameters was performed: (a) number of portal spaces/glomeruli, (b) any fragment > 5 mm present and (c) any fragment > 10 mm present.

Statistical analysis

Continuous variables are presented with mean and standard deviation (SD). Qualitative variables are presented with absolute and relative frequencies. Differences in weight of the biopsies and number of portal spaces among the different calibre sizes and between the three systems were evaluated using repeated measurements analysis of variance (ANOVA). For the comparison of proportions, chi-square and Fisher's exact tests were used. The Bonferroni correction was used in post hoc comparisons in order to control type I error. All p values reported are two-tailed. Statistical significance was set at 0.05, and analyses were conducted using SPSS statistical software (version 19.0).

Results

Mean weight of the biopsies according to system and calibre sizes in the total sample and separately for kidney and liver tissues are presented in Table 2. Significantly greater weight was found in 14G size as compared to 16G and 18G in all systems. Also, the mean weight of the biopsies was significantly greater in 16G size as compared to 18G in all systems. The aforementioned results were consistent in the total sample and separately in liver and kidney biopsies. Concerning kidney biopsies and 14G size, a significantly greater weight was found in system A as compared to system C. Concerning liver biopsies and 14G, 18G sizes, a significantly greater weight, was found in system A as compared to systems B and C. In total sample of biopsies, the mean weight was greater in system A as compared to systems B and C in 14G and 16G sizes. Additionally, in the total sample, the mean weight was greater in system A as compared to system C in 18G size.

Table 3 shows the mean number of glomeruli, portal spaces and proportions of fragments over 5 mm or over 10 mm, according to system and calibre sizes in the total sample and separately for kidney and liver tissues. The mean number of both glomeruli and portal spaces was greater in 14G size as compared to 18G in

Table 1 Micro-mechanical characteristics of the three needle systems

System A	System B	System C
14G	14G	14G
1. 2.05 mm Ø	1. 2.10 mm Ø	1. 2.10 mm Ø
2. 1.71 mm Ø	2. 1.73 mm Ø	2. 1.77 mm Ø
3. 0.60 mm	3. 0.53 mm	3. 0.59 mm
4. 1.11 mm (no. 2–no. 3)	4. 1.20 mm (no. 2–no. 3)	4. 1.18 mm (no. 2–no. 3)
5. 19.04 mm (only flat part)	5. 16.00 mm (only flat part)	5. 15.30 mm (only flat part)
16G	16G	16G
1. 1.62 mm Ø	1. 1.57 mm Ø	1. 1.73 mm Ø
2. 1.30 mm Ø	2. 1.29 mm Ø	2. 1.34 mm Ø
3. 0.53 mm	3. 0.56 mm	3. 0.45 mm
4. 0.77 mm (no. 2–no. 3)	4. 0.73 mm (no. 2–no. 3)	4. 0.89 mm (no. 2–no. 3)
5. 19.74 mm (only flat part)	5. 17.12 mm (only flat part)	5. 16.20 mm (only flat part)
18G	18G	18G
1. 1.17 mm Ø	1. 1.25 mm Ø	1. 1.22 mm Ø
2. 0.90 mm Ø	2. 0.97 mm Ø	2. 0.97 mm Ø
3. 0.40 mm	3. 0.49 mm	3. 0.31 mm
4. 0.50 mm (no. 2–no. 3)	4. 0.48 mm (no. 2–no. 3)	4. 0.66 mm (no. 2–no. 3)
5. 18.07 mm (only flat part)	5. 17.34 mm (only flat part)	5. 16.25 mm (only flat part)

systems A and C of kidney and liver biopsies, as well as in the total sample. Also, the mean number of glomeruli was greater in 16G size as compared to 18G size in system C of kidney biopsies. In liver biopsies, the mean number of portal spaces was greater in 16G size as compared to 18G in systems B and C, while in system A, it was greater in 14G size as compared to

Table 2 Mean weight of the biopsies according to system and calibre sizes in total sample and separately for kidney and liver tissues

	Calibre sizes			*p* value		
	14G Mean (SD)	16G Mean (SD)	18G Mean (SD)	14 vs. 16	14 vs. 18	16 vs. 18
Kidney						
System A	19.7 (3.2)	12 (1.7)	6.2 (2.4)	< 0.001	< 0.001	< 0.001
System B	18.3 (5.3)	9.1 (2.2)	5.2 (1.3)	< 0.001	< 0.001	< 0.001
System C	13.7 (3.6)	10.1 (3.8)	3.8 (2.9)	0.033	< 0.001	< 0.001
P (A vs. B)	0.839	0.068	0.720			
P (A vs. C)	0.009	0.333	0.085			
P (B vs. C)	0.056	0.798	0.470			
Liver						
System A	23.3 (4.7)	11.6 (2.1)	5.4 (0.8)	< 0.001	< 0.001	< 0.001
System B	17.0 (3.6)	10.4 (1.7)	3.7 (1.2)	< 0.001	< 0.001	< 0.001
System C	16.9 (2.3)	9.7 (2.4)	3.6 (1.7)	< 0.001	< 0.001	< 0.001
P (A vs. B)	0.002	0.496	0.019			
P (A vs. C)	0.002	0.140	0.013			
P (B vs. C)	> 0.999	0.838	0.997			
Total						
System A	21.5 (4.3)	11.8 (1.9)	5.8 (1.8)	< 0.001	< 0.001	< 0.001
System B	17.7 (4.5)	9.8 (2)	4.5 (1.4)	< 0.001	< 0.001	< 0.001
System C	15.3 (3.4)	9.9 (3.1)	3.7 (2.3)	< 0.001	< 0.001	< 0.001
P (A vs. B)	0.012	0.025	0.084			
P (A vs. C)	< 0.001	0.042	0.003			
P (B vs. C)	0.204	0.996	0.521			

Table 3 Mean number of glomeruli, portal spaces and proportions of fragments > 5 mm or > 10 mm according to system and calibre sizes in total sample and separately for kidney and liver tissues

	14G	16G	18G	*p* value		
				14 vs. 16	14 vs. 18	16 vs.18
Kidney						
No of glomeruli, mean (SD)						
System A	12.8 (7.9)	10.9 (7.7)	5.3 (3.7)	0.851	0.050	0.075
System B	8.2 (8.8)	6.3 (6.4)	8.1 (7.0)	0.851	> 0.999	0.837
System C	11 (9.7)	10 (9.8)	3.5 (4.1)	0.974	0.050	0.032
Any fragment > 5 mm, *N* (%)						
System A	10 (100)	10 (100)	10 (100)	–	–	–
System B	10 (100)	10 (100)	10 (100)	–	–	–
System C	10 (100)	9 (90)	7 (70)	> 0.999	0.633	> 0.999
Any fragment > 10 mm, *N* (%)						
System A	8 (80)	10 (100)	5 (50)	> 0.999	> 0.999	0.098
System B	7 (70)	7 (70)	7 (70)	> 0.999	> 0.999	> 0.999
System C	6 (60)	5 (50)	5 (50)	> 0.999	> 0.999	> 0.999
Liver						
No of portal spaces, mean (SD)						
System A	8.6 (1.9)	4.5 (2.5)	3.3 (2.2)	0.001	< 0.001	0.448
System B	5.6 (3.0)	5.9 (2.3)	3.7 (1.9)	0.987	0.137	0.050
System C	6.3 (1.7)	5.9 (1.4)	2.1 (1.3)	0.970	< 0.001	0.001
Any fragment > 5 mm, *N* (%)						
System A	10 (100)	10 (100)	6 (60)	–	0.261	0.261
System B	10 (100)	10 (100)	8 (80)	–	> 0.999	> 0.999
System C	10 (100)	10 (100)	2 (20)	–	0.003	0.003
Any fragment > 10 mm, *N* (%)						
System A	7 (70)	6 (60)	2 (20)	> 0.999	0.210	0.510
System B	5 (50)	4 (40)	2 (20)	> 0.999	> 0.999	> 0.999
System C	5 (50)	6 (60)	0 (0)	> 0.999	0.098	0.033
Total sample						
No of portal spaces, mean (SD)						
System A	10.7 (6)	7.7 (6.5)	4.3 (3.1)	0.093	< 0.001	0.034
System B	6.9 (6.6)	6.1 (4.7)	5.9 (5.5)	0.915	0.887	0.998
System C	8.6 (7.2)	8 (7.1)	2.8 (3.0)	0.941	0.001	0.001
Any fragment > 5 mm, *N* (%)						
System A	20 (100)	20 (100)	16 (80)	–	0.318	0.318
System B	20 (100)	20 (100)	18 (90)	–	> 0.999	> 0.999
System C	20 (100)	19 (95)	9 (45)	> 0.999	< 0.001	< 0.001
Any fragment > 10 mm, *N* (%)						
System A	15 (75)	16 (80)	7 (35)	> 0.999	0.033	0.012
System B	12 (60)	11 (55)	9 (45)	> 0.999	> 0.999	> 0.999
System C	11 (55)	11 (55)	5 (25)	> 0.999	0.159	0.159

16G size. In the total sample of biopsies, the mean number of glomeruli/ portal spaces was greater in 16G size as compared to 18G in systems A and C. Concerning comparisons of number of glomeruli/portal spaces between the three systems in total sample, the only difference that was found was the greater mean number in system A as compared to B in 14G size (Fig. 2a, b).

All kidney biopsies in systems A and B had fragments over 5 mm. The proportion of kidney biopsies with fragments over 5 mm in kidney was not significantly different among the different sizes or between the three systems. The proportion of kidney biopsies with fragments over 10 mm was not significantly different among the different sizes, but it was greater in system A as compared to system C in 16G size. A greater proportion of biopsies with fragments over 5 mm was detected in 14G and 16G sizes as compared to 18G size, in system C of liver and total sample biopsies. In both liver and the total sample biopsies, the

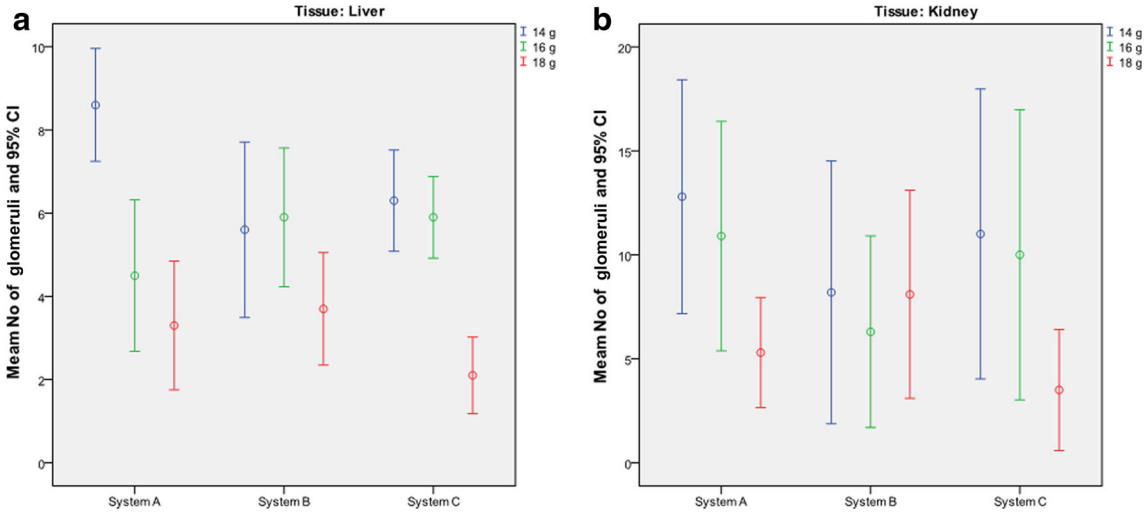

Fig. 2 **a** Mean number of portal spaces according to system and caliber sizes in total sample. **b** Mean number of glomeruli according to system and calibre sizes in total sample

proportion of fragments over 5 mm that were found was greater in system B as compared to system C of 18G size. In liver biopsies, the proportion of fragments over 10 mm was greater in 16G size as compared to 18G size of system C. In the total sample biopsies, the proportion of fragments over 10 mm was greater in 14G and 16G sizes as compared to 18G size of system A.

Discussion

The main techniques used for tissue biopsy are the use of fine needle aspiration (FNA) with a needle from 20G to 25G that offers cytologic assessment mainly based on morphologic analysis and core biopsies that are performed with needle systems between 14G and 20G and offer information regarding the architectural features of the tissue. Both techniques are reliable; therefore, they have been used without significant change for many years [1, 3, 4].

The new challenge for percutaneous biopsies is to be able to follow the pace of evolution of personalised medicine, particularly after the introduction of liquid biopsies. The latter generated a lot of initial excitement in the world of oncology as it appeared as a less invasive for the detection tumour heterogeneity, being able to analyse the fragments of the circulating DNA [5]. However, the technology of liquid biopsies is still emerging, and liquid biopsies cannot provide significant information for personalised medicine like for example the characterisation of the tumour micro-environment. There is a continuous trend from commercial laboratories to perform sophisticated genomic testing. Most of the laboratories will come with specific requirements on the amount of tissue required (mainly expressed as the weight of the tissue); therefore, interventional radiologists should be knowledgeable on which biopsy needle system will satisfy the required criteria. Furthermore, the design of future biopsy systems should take into account information on how to achieve tissue weight for the same needle calibre.

This laboratory study is designed on that purpose. It is aiming to evaluate the results of three popular biopsy systems in terms of quantity and quality of the obtained sample and to assess the specific needle micro-mechanical characteristics that influence this result. Sample biopsies were obtained from animal organs that resemble human ones.

Based on the experience of histology, the aim of percutaneous biopsies is to obtain a diagnostic quantity of tissue with the lowest number of capsular passes in order to reduce complications. And this is expected to be achieved with a larger diameter needle. Peters et al [6], in a recent study of 1299 patients that underwent background biopsies for transplant (260) and native (1039) kidneys, demonstrated better results of the 16G system in comparison to the 18G. The mean number of glomeruli obtained per pass was 11 vs. 8 for the two systems, respectively, with a statistically significant difference ($p < 0.001$). This result was confirmed in our experiment for both the kidneys and livers. The mass obtained from all the 14G systems was higher than the mass of tissue obtained from all the 16G systems, and the mass obtained from all the 16G was higher than that obtained from all the 18G with a statistically significant superiority. In addition, Roth et al [7] confirmed that even though there is a trend to use smaller calibre needle systems in order to reduce bleeding complications, there is a number of biopsies—particularly those obtained with very small needle systems, i.e. 20G or 22G—that lead to inadequate tissue sampling and non-diagnostic results.

Furthermore, it is also a common belief that same calibre needle systems, with the same needle throw, will obtain the same amount and the same quality of tissue. However, this is not true. This study elucidated which features of needle systems micro-architecture increase needle performance in percutaneous liver and kidney biopsies. The systems that were

assessed differed in the following characteristics: (a) needle external diameter ranging from 2.05 to 2.10 mm for the 14G systems, 1.57 mm to 1.73 mm for the 16G and 1.17 mm to 1.25 mm for the 18G, (b) needle tray height ranging from 1.11 to 1.18 mm for the 14G systems, 0.73 mm to 0.89 mm for the 16G and 0.48 mm to 0.66 mm for the 18G and (c) effective needle tray length, ranging from 15.3 to 19.04 mm for the 14G systems, 16.2 mm to 19.74 mm for the 16G and 16.25 mm to 18.07 mm for the 18G. The clinical indications of use are the same for all the three systems, and there are no specific applications where one of the three systems is highly used in respect to the other two. The respective manufacturers provide the micro-mechanical characteristics of the needle systems. The system that appeared to perform better was the one with the longest effective needle tray (system A), measuring 19.04 mm, 19.74 mm and 18.07 mm for 14G, 16G and 18G, respectively. Another characteristic of system A is that it was an automatic one, but this factor does not appear to play any significant role considering that system B was semi-automatic and system C was an automatic system. The rationale behind choosing these three specific needle systems was based on the popularity that the systems have in our experience. It is worth underlying that other needle systems may produce different results in the same experimental setup.

The main limitations of this study are the fact that only three needle systems were used and the fact that the experiment was performed in an ex vivo model where explanted organs are not expected to be as firm as in vivo tissue. We believe this inevitably conditions the fragmentation rate and the overall quality of the samples. Another limitation is the fact that the study was not performed on tumours and, therefore, the conclusions may not be applicable to tumour biopsies.

A factor that was not taken into account in this ex vivo study is the weight of the system or any other practical issues that may influence the decision of many operators. However, when it comes to tissue sampling, the parameter that plays the most important role is the amount and the quality of the obtained tissue, particularly when this is performed in view of genomic testing.

We may conclude, from the ex vivo model, that the factor that appears to influence the quantity and quality of the obtained background kidney and liver tissue appears to be the effective needle tray length and not the needle external diameter or even the needle tray height. This information needs to be taken into account in the future design of biopsy needle systems.

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Compliance with ethical standards

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Statistics and biometry Dr. Chara Tzavara kindly provided statistical advice for this manuscript.

Informed consent Approval from the institutional animal care committee was not required because the study was performed ex vivo.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Prospective
- Experimental
- Performed at one institution

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