

**Ultrasound-Guided Percutaneous Liver Biopsy
A Review on Obtaining Adequate Specimens**

de Lange, Danny; Van Den Dobbelseen, John J.; Moelker, Adriaan; Van De Berg, Nick J.

DOI

[10.1115/1.4047543](https://doi.org/10.1115/1.4047543)

Publication date

2020

Document Version

Final published version

Published in

Journal of Medical Devices, Transactions of the ASME

Citation (APA)

de Lange, D., Van Den Dobbelseen, J. J., Moelker, A., & Van De Berg, N. J. (2020). Ultrasound-Guided Percutaneous Liver Biopsy: A Review on Obtaining Adequate Specimens. *Journal of Medical Devices, Transactions of the ASME*, 14(3), Article 034503. <https://doi.org/10.1115/1.4047543>

Important note

To cite this publication, please use the final published version (if applicable).
Please check the document version above.

Copyright

Other than for strictly personal use, it is not permitted to download, forward or distribute the text or part of it, without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license such as Creative Commons.

Takedown policy

Please contact us and provide details if you believe this document breaches copyrights.
We will remove access to the work immediately and investigate your claim.

Ultrasound-Guided Percutaneous Liver Biopsy: A Review on Obtaining Adequate Specimens

Danny de Lange

Department of BioMechanical Engineering,
Delft University of Technology,
Mekelweg 2,
Delft 2628CD, The Netherlands
e-mail: danny22_03@hotmail.com

John J. van den Dobbelsteen

Department of BioMechanical Engineering,
Delft University of Technology,
Mekelweg 2,
Delft 2628CD, The Netherlands
e-mail: j.j.vandendobbelsteen@tudelft.nl

Adriaan Moelker

Erasmus MC,
Department of Radiology and Nuclear Medicine,
Doctor Molewaterplein 40,
Rotterdam 3015 GD, The Netherlands
e-mail: a.moelker@erasmusmc.nl

Nick J. van de Berg

Erasmus MC,
Department of Radiology and Nuclear Medicine,
Doctor Molewaterplein 40,
Rotterdam 3015 GD, The Netherlands;
Department of BioMechanical Engineering,
Delft University of Technology,
Mekelweg 2,
Delft 2628CD, The Netherlands
e-mail: n.j.p.vandenberg@tudelft.nl

This literature review was conducted to evaluate liver biopsy adequacy, including total core length (TCL), number of portal tracts (PT), fragmentation, and complication rates, as a function of needle type and gauge. A systematic electronic search was performed in the Web of Science and Google Scholar databases, according to the PRISMA statement. Eligible data, describing in vivo percutaneous ultrasound-guided human liver biopsy quality outcomes, were compared to adequacy criteria of the American Association for the Study of Liver Diseases (AASLD, $TCL \geq 20$ mm, $PT \geq 11$). An adequate mean number of PTs was found in 83% of biopsy needles assessed between 2012 and 2019, compared to 0% between 1998 and 2004. For TCL, this was 44% and 33%, respectively. Increasing the needle diameter enhanced TCL (result in 50% of included studies) and PT count (100%), and reduced fragmentation rates (75%), whereas no effect on pain or complications was found (83%). In total, five needle types achieved adequate PT counts, using 16G (3 \times), 17G (1 \times), or 18G (1 \times) needles. Adequacy was reached using either a core needle biopsy (CNB, 3 \times) approach with one pass, or a fine needle aspiration (FNA, 2 \times) approach with two passes. The recommendations for biopsy adequacy can be met using 16/17G FNA or 16/18G CNB needles. Currently, many publications still present substandard

liver biopsy quality outcomes. Although minimizing biopsy invasiveness is desirable, a decreased diameter or number of passes is ill-judged when reliability of biopsy outcomes is at stake.
[DOI: 10.1115/1.4047543]

Introduction

Liver biopsy is a gold standard in the diagnostic management of hepatic diseases [1–6], and is recommended by the *American Association for the Study of Liver Diseases* (AASLD) when diagnosis is in question, when specific diagnostic information can alter management plans, or when prognostic information, e.g., about fibrosis stage, can guide subsequent treatment [2]. Percutaneous liver biopsy can be divided in core needle biopsy (CNB) and fine needle aspiration (FNA), making use of (semi)-automated spring-loaded shooting mechanisms and suction functionality, respectively.

Correct diagnosis of hepatic diseases requires evaluation of a sufficient amount of parenchyma and number of portal tracts (PT), i.e., specimens need to be of sufficient quality and size. For instance, biopsy size is crucial to accurately grade and stage chronic viral hepatitis [7]. Therefore, total core length (TCL) [8–10] and fragmentation rates are often disclosed. It should be known that TCL measures differently for interventional radiologists and pathologists, as the gathered tissue is subject to shrinkage during formalin fixation [2]. Recently, the role of tissue sampling has increased tremendously as a result of the expanding interest in personalized medicine, pursuing diagnostic, and therapeutic biomarkers for stratifying patients into those who may or may not respond to treatment. For this application, adequacy relates to present cell numbers, proportion of diagnostic (e.g., tumor) cells and the amounts of ribonucleic acid, DNA, or protein markers [11]. Distinct quantitative recommendations still have to be defined in this field.

Used liver biopsy adequacy thresholds differ between studies and range from 15–30 mm to 6–11, for TCL and PT counts, respectively [7–10,12–14]. Recommendations of the AASLD include a minimum TCL of 20–30 mm, the use of 16G needles, and pathology report notations in case fewer than 11 complete PTs were found [2]. Based on these values, specimens are defined as either *inadequate* ($PT < 6$, $TCL < 15$ mm), *compromised* ($PT < 11$, $TCL < 20$ mm), or *adequate* ($PT \geq 11$, $TCL \geq 20$ mm) [15].

The aim of this review was to compare specimen adequacy in terms of TCL, PT numbers, and fragmentation, as a function of biopsy needle type and gauge. In addition, pain and complication rates were reviewed. In 2006, Cholongitas et al. [10] reviewed percutaneous liver biopsy specimen quality. At that time, none of the documented series of biopsies in literature met adequacy criteria. Our goal was to analyze whether this is still true and if particular needle types or sizes provide superior outcomes.

Methods

Search Strategy. This systematic review was written following the checklist of the PRISMA statement [16]. A comprehensive electronic search was performed in databases of Web of Science and Google Scholar, using the search terms: liver, needle, biopsy, FNA, CNB, in combination with the Boolean operators AND/OR. Search limits included publishing date (1998–2019, last updated on November 19, 2019) and language (English). The relevance of identified records ($n = 357$), as well as additional records obtained through citation chaining ($n = 10$), was determined by the first author by analyzing titles and abstracts and screening full texts. Remaining articles were assessed and subjected to exclusion and inclusion criteria (Fig. 1).

Article Inclusion. To enable comparison of biopsy devices between studies, narrow inclusion criteria were imposed. All data resulted from in vivo percutaneous biopsies in human livers, excluding transjugular, endoscopic (EUS), and open approaches. All specimens were attained with ultrasound guidance. Exclusion also encompassed confounding study objectives, e.g., studying of

Manuscript received December 9, 2019; final manuscript received June 2, 2020; published online July 16, 2020. Assoc. Editor: Xiaoming He.

fanning techniques to collect more tissue or grouping of inexperienced operators. In addition, inclusion required exact delineation of devices used. Clustered data, containing multiple or unspecified needle types or diameters, were excluded. Finally, to enable comparison of results, data summary using means and standard deviations (SD) was required.

Data Extraction. Relevant data were extracted by means of the population, intervention, comparison, and outcome (PICO) system, stated in Cochrane Handbook for Systematic Reviews [17]. Extracted information included type of biopsy needle, number of patients, type of disease or lesion, number of portal tracts, total core lengths, fragmentations, and complication rates. Data summary metrics were computed using MATLAB (R2019a, MathWorks, Natick, MA). Included studies were summarized by *p*-values and statistical tests, e.g., Student’s *t*-test and Fisher’s exact test for numerical and categorical data, respectively. All significance levels were set to $\alpha = 0.05$. As a result of strict inclusion criteria, the number of articles was insufficient for statistical meta-analysis. Findings were summarized using the means \pm SDs of extracted data.

Results

Study Characteristics. In total, nine studies (out of 61) met inclusion criteria. Five were published between 1998 and 2004

[18–22], and four between 2012 and 2019 [15,23–25]. A total of 13 needles was found within these studies (Table 1). Needle diameters ranged between 21 and 16 G (0.8–1.7 mm). A selection of included needle tips is shown in Fig. 2.

Total Core Length. Mean observed TCL was adequate in 40% (6/15), compromised in 20% (3/15), and inadequate in 40% (6/15) of cases (Fig. 3). Adequate biopsies were achieved with Menghini FNA needles [19,21], and with Biopince and achieve CNB needles [15].

Effect of Needle Gauge. Effect of needle gauge on TCL of specimens was investigated in six studies. Two studies found that larger diameter needles provided longer specimens [15,21]. One found that the fraction of specimens longer than 5 mm increased [26]. In two studies, a clear relation between needle gauge and specimen length was not found [19,24]. Longer specimens were obtained with smaller diameter needles in one study [25].

Röcken et al. [19] studied needle insertion by physicians and surgeons and evaluated the effect of “single pass” and “fanning” techniques. The TCL increased using fanning techniques (TCL = 39.4 ± 17.4 mm). Single pass biopsies were executed with 17 G, 20 G, and 21 G Menghini needles. The highest TCL was found for 20 G needles (TCL = 29.8 ± 12.9 mm), followed by

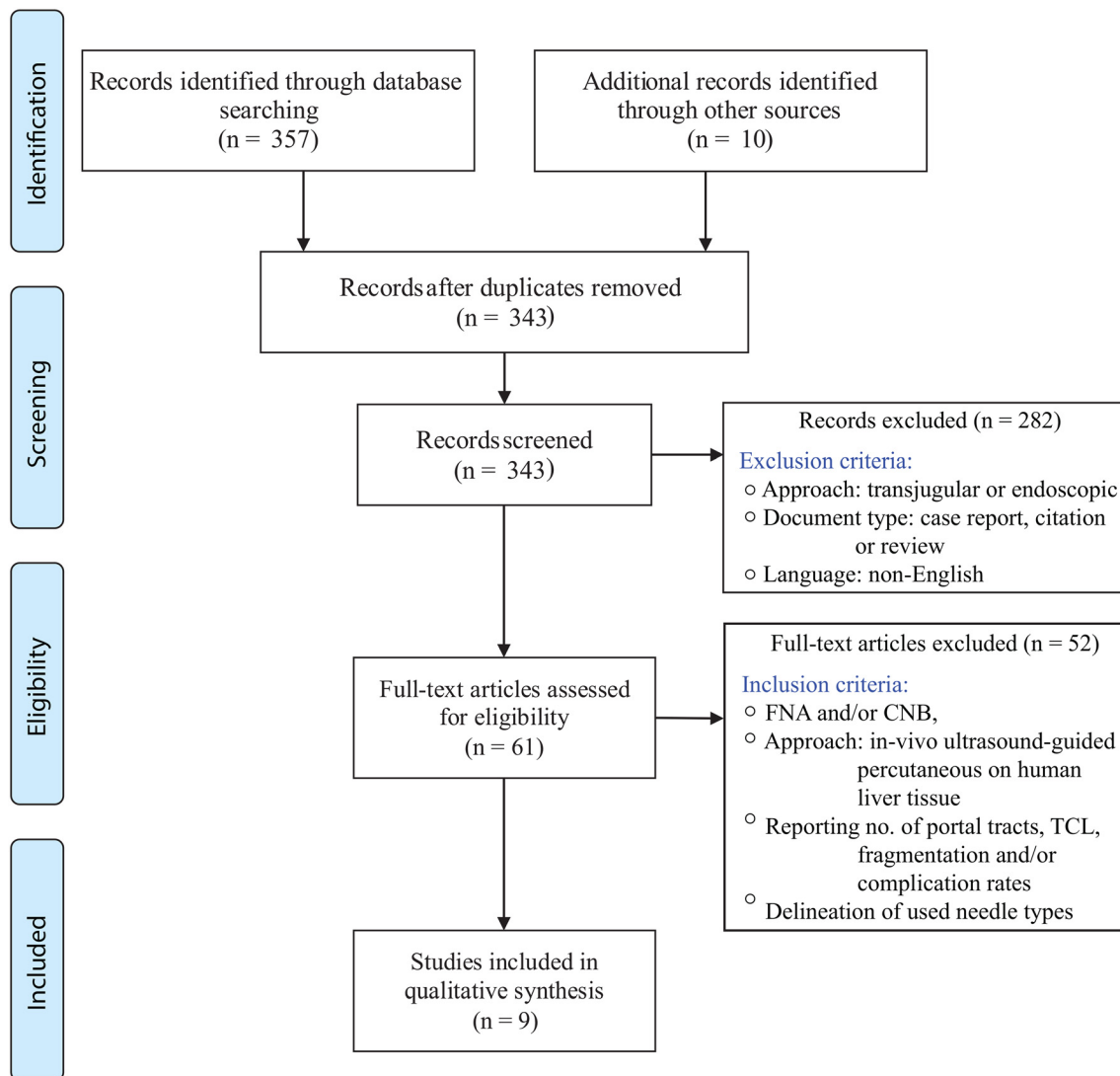


Fig. 1 PRISMA Flow diagram of the systematic literature search, indicating inclusion and exclusion criteria and number of articles remaining

Table 1 Summary of needle types and research study variables

Product	Company	Biopsy type	Needle tip	Needle gauge	No. of biopsies	No. of passes	Aetiology	Ref.
Achieve	Argon Medical (Frisco, TX)	CNB	Bevel, side-notch	18	141	—	Parenchymal liver disease	[15]
Biomol	Hospital Service (Rome, Italy)	FNA	Menghini	21	149	1	Diffuse liver disease	[21]
Biopince	CareFusion (Illinois, IL)	CNB	Tri-axial tip, end-cut	16	53	—	Parenchymal liver disease	[15]
Biopsy Gun	Bard (Covington, GA)	CNB	Bevel, side-notch	18	78	1.3	—	[18]
Gallini	Gallini (Modena, Italy)	CNB	Bevel, side-notch	18	449	1	Various	[22]
Hepa-cut	Sterylab (Rho, Italy)	FNA	Menghini	18	149	1	Diffuse liver disease	[21]
Hepafix	B. Braun (Melsungen, Germany)	FNA	Menghini	16, 17	516, 80	2	Chronic diffuse liver diseases	[23]
			Menghini	17, 20, 21	79, 98, 97	1		[19]
Max-Core	Bard (Covington, GA)	CNB	Bevel, side-notch	16, 18	75, 75	1	Diffuse liver disease	[25]
Monoptoy	Bard (Covington, GA)	CNB	Bevel, side-notch	16	58	1	Chronic hepatitis C virus infection	[20]
QuickCore	Cook Medical Inc. (Bloomington, IN)	CNB	Bevel, side-notch	18	48	1	Ex vivo nondiseased liver	[28]
SharkCore ^a	Medtronic (Dublin, Ireland)	EUS-FNB	Opposing bevel	19, 22	48, 48	1	Ex vivo nondiseased liver	[28]
Surecut	—	FNA	Menghini	18	67	1.6	—	[18]
Temno	Cardinal Health (Dublin, OH)	CNB	Bevel, side-notch	18, 20	722, 49	2, 3	Parenchymal liver disease	[24]
	CareFusion (Illinois, IL)	CNB	Four-sided bevel, side-notch	18	48	1	Ex vivo nondiseased liver	[28]

^aEUS needle (data not included in analysis) to which other percutaneous needles were statistically compared.

17 G (TCL = 25.3 ± 11.3 mm), and 21 G (TCL = 22.1 ± 12.7 mm) needles (ANOVA, $p < 0.05$).

Vijayaraghavan et al. [24] found no difference in mean TCL of 90 mm long, 18 G (TCL = 14.4 ± 3.7 mm) and 20 G (TCL = 14.1 ± 3.4 mm) Temno needles (Wilcoxon–Mann–Whitney, $p = 0.5$), using a median of 2 and 3 passes, respectively. Number of passes depended on visual specimen inspection by the radiologist.

Tublin et al. [25] found a significantly different mean TCL in single pass biopsies of 18 G (TCL = 19 mm) and 16 G (TCL = 17 mm) CNB needles (Student’s t -test, $p = 0.03$).

Two studies simultaneously varied needle gauge and brand. Hall et al. [15] found a significantly higher mean TCL using 16 G Biopince (TCL = 23 ± 4.1 mm), versus 18 G Achieve (TCL = 20 ± 6.8 mm) CNB needles (Student’s t -test; $p < 0.01$). Brunetti et al. [21] found a significantly higher mean TCL using 18 G Hepa-cut (TCL = 21.2 mm), versus 21 G Biomol (TCL = 12.2 mm) FNA needles (Student’s t -test, $p < 0.01$).

Effect of Needle Type. The effect of needle type on TCL was evaluated in two studies. Sparchez et al. [18] compared 18 G Menghini Surecut (TCL = 12.5 ± 3.6 mm) and 18 G Biopsy Gun

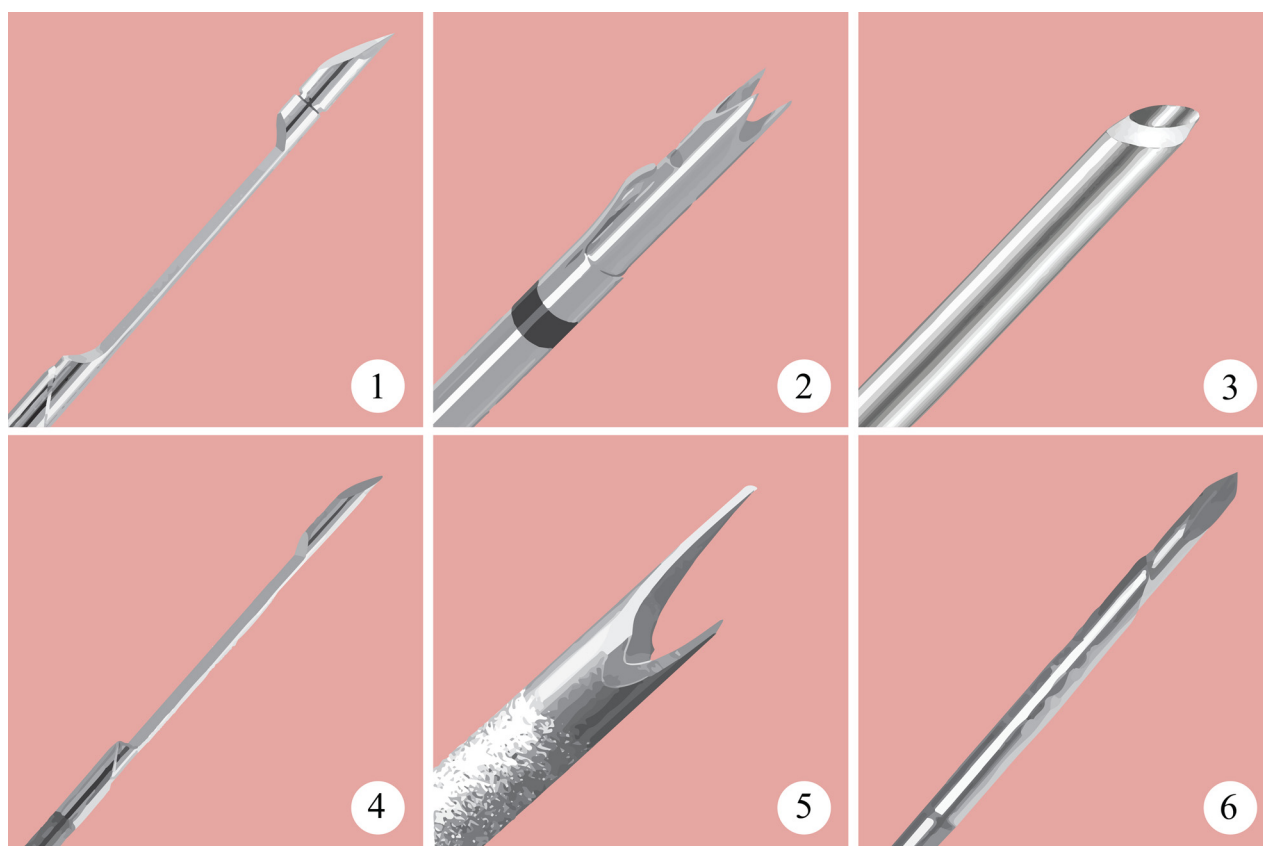


Fig. 2 Selection of exemplar biopsy needle types: (1) achieve, CNB with bevel tip, (2) Biopince, CNB, (3) Hepafix, Menghini, (4) Monoptoy, CNB with bevel tip, (5) SharkCore, opposing bevel, and (6) Temno, CNB with centered tip

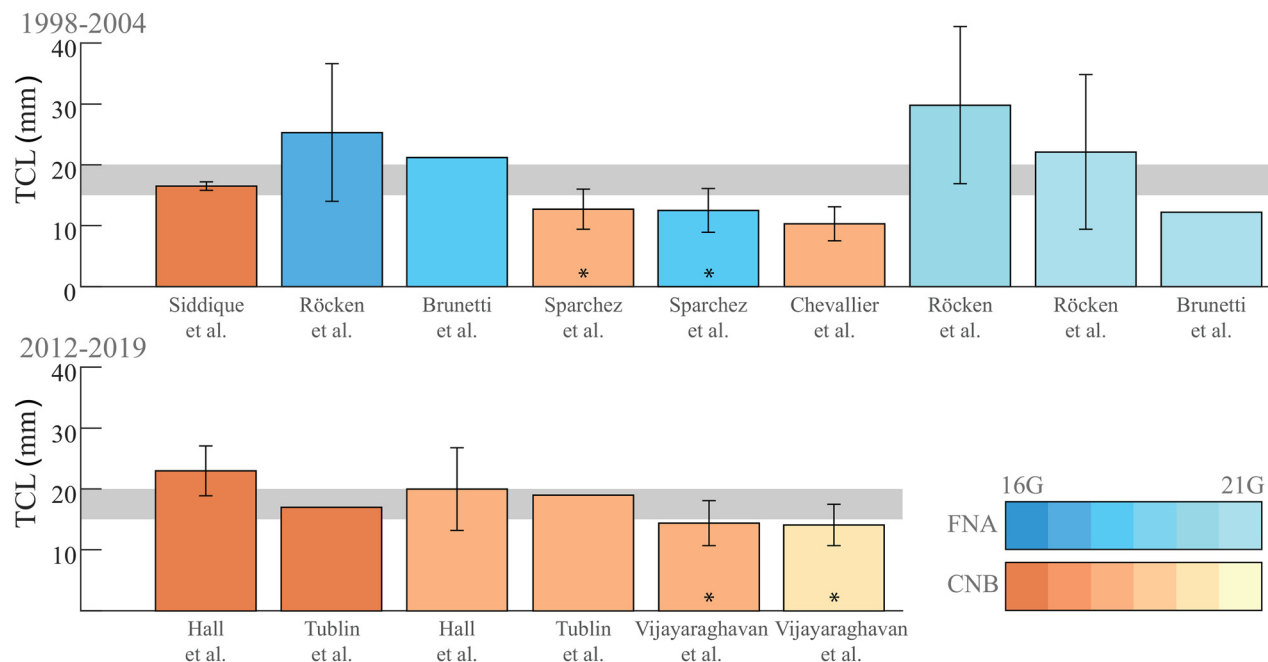


Fig. 3 Overview of mean TCLs of liver biopsies acquired with FNA or CNB needles, in the time periods 1998–2004 and 2012–2019. Face color intensities of bars indicate the needle gauge (16–21 G) and the gray band indicates a compromised adequacy with TCL values ranging between 15 and 20 mm. An asterisk denotes a mean number of passes > 1.

(TCL = 12.7 ± 3.3) needles (p = not significant). However, required mean number of needle passes was varied simultaneously and was 1.6 and 1.3, respectively ($p < 0.05$, test not specified). Li et al. [26] presented the fraction of specimens with a TCL > 5 mm. A significantly larger fraction was obtained with 18 G Tru-Cut CNB (82.6%), compared to 21 G Hakko FNA (52.1%) needles (Student's t -test, $p < 0.01$).

Number of Portal Tracts. When comparing obtained number of PTs, 38% (5/13) was adequate, 46% (6/13) was compromised, and 15% (2/13) was inadequate (Fig. 4). Adequate biopsies were not achieved in the 1998–2004 studies. Between 2012 and 2019, adequate biopsies were achieved in two passes using 16/17 G Hepafix Menghini-modified needles [23], and in one pass using 16 G Biopince and 16/18 G Max-Core CNB needles [15,25].

Effect of Needle Gauge. The effect of needle gauge on number of complete PTs in biopsy specimens was investigated in four studies [15,19,23,25]. All four studies found a statistically larger number of PTs for needles with a smaller gauge.

Röcken et al. [19] found that number of PTs obtained with 17 G (PT = 9.7 ± 5.9), 20 G (PT = 6.7 ± 4.4), and 21 G (PT = 4.0 ± 3.1) Menghini needles, differed (ANOVA, $p < 0.05$). Six or more portal tracts were obtained in 70%, 58%, and 25% of tissue samples, respectively.

Sporea et al. [23] found more PTs with 16 G Menghini (PT = 24.6 ± 10.6), compared to 17 G Menghini (PT = 20.8 ± 8.6) needles (Mann Whitney U test, $p < 0.01$). All specimens were acquired with two passes. The larger 16 G needle was used when liver cirrhosis was suspected to minimize the risk on tissue fragmentation.

Tublin et al. [25] acquired more PTs in single pass biopsies with 16 G (PT = 14) compared to 18 G (PT = 13) CNB needles (Student's t -test, $p = 0.03$).

One study simultaneously varied needle gauge and brand. Hall et al. [15] obtained more PTs with 16 G Biopince (PT = 11 ± 4.2) than with 18 G Achieve (PT = 7 ± 3.4) needles (Student's t -test, $p < 0.01$). They characterized adequacy (PT ≥ 11 , TCL ≥ 25 mm), and reached this in 31.3% and 1.3% of cases, respectively (Student's t -test, $p < 0.01$).

Effect of Needle Type. Sporea et al. [27] performed a multicenter study to compare the number of PTs of TruCut and Menghini needles. Used needle diameters were not mentioned. Discussed are effects of junior and senior operators. A number of portal tracts found in specimens collected in four hospitals by senior operators (>100 liver biopsies) were 8.6 ± 4.8 and 10.3 ± 3.6 (Menghini, single pass), 20.8 ± 10.1 (Menghini, double pass), and 12.1 ± 5.9 (Tru-Cut, single pass).

Sparchez et al. [18] found no differences in PT numbers in biopsies acquired with 18 G Menghini Surecut (PT = 7.2 ± 3.1) and 18 G Biopity Gun (PT = 8.1 ± 4.3) needles.

Schulman et al. [28] compared EUS-guided biopsy needles with two percutaneous CNB needles in human cadaveric tissue. The difference in single pass yields of percutaneous 18 G Quick-Core (PT = 2.5) and 18 G Coaxial Temno (PT = 3.4) needles was not statistically tested. The 19 G SharkCore (PT = 4.1) needle (Fig. 2) provided more portal tracts than the QuickCore needle (Student's t -test, $p = 0.04$). The SharkCore and Temno needles did not differ significantly. The 19 G SharkCore needle was also used in a three-pass technique, resulting in an average 6.2 portal tracts.

Fragmentation. The relation between needle gauge and fragmentation (F) of biopsy specimens was analyzed in four studies (Fig. 5). A lower percentage of fragments for needles with a smaller gauge was found in three of the four studies [15,19,21]. One study found no relation between needle gauge and fragmentation [28]. Relations between needle type (FNA/CNB) and fragmentation could not be properly studied with available data. However, there are concern for fragmentation caused by FNA suction forces, particularly in cirrhotic livers [2].

Röcken et al. [19] compared Menghini needles with three diameters. They found a significantly lower percentage of fragments in samples obtained with 17 G ($F = 9\%$), compared to 21 G ($F = 24\%$) needles (ANOVA, $p < 0.01$). Specimens obtained with an intermediate 20 G ($F = 15\%$) needle did not differ from the 17 G and 21 G groups.

Two studies simultaneously varied needle gauge and brand. Hall et al. [15] found a significantly lower percentage of

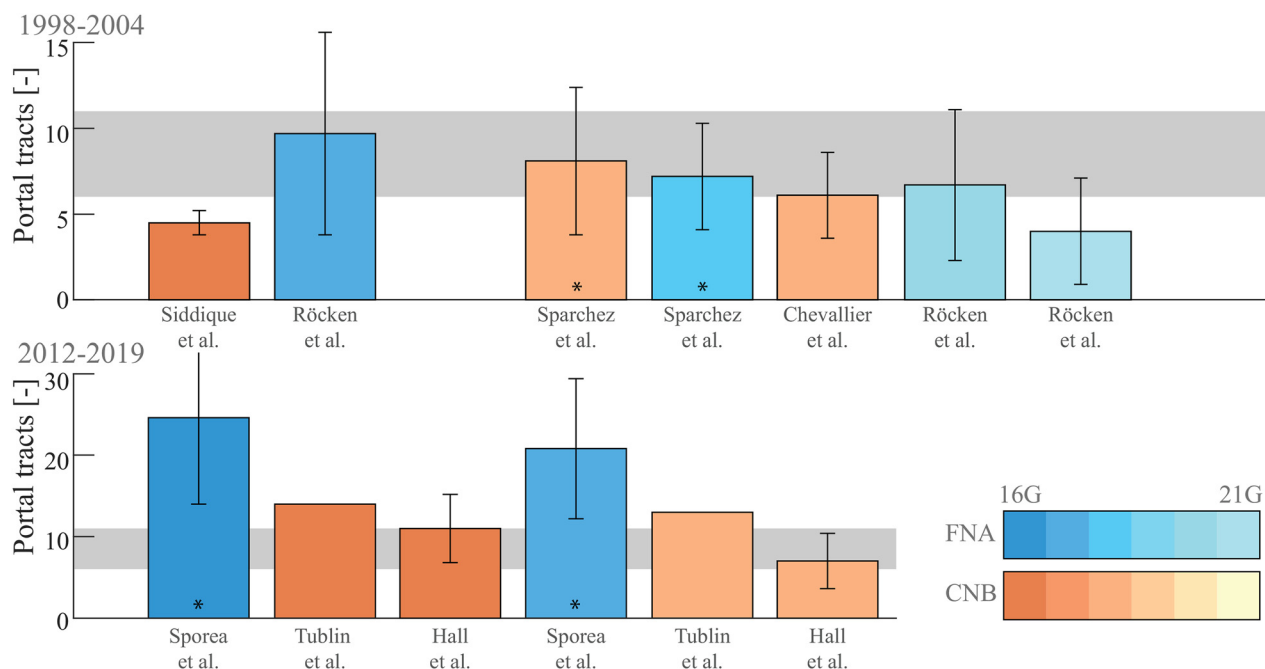


Fig. 4 Overview of mean number of PTs of liver biopsies acquired with FNA or CNB needles, in the time periods 1998–2004 and 2012–2019. Face color intensities of bars indicate the needle gauge (16–21 G) and the gray band indicates a compromised adequacy with number of PTs ranging between 6 and 11. An asterisk denotes a mean number of passes > 1.

fragmented samples using the 16 G Biopince ($F = 1.8\%$), compared to the 18 G Achieve ($F = 28.1\%$) CNB needles (Student's t -test; $p < 0.01$). Brunetti et al. [21] found a significantly lower percentage of fragmentation using the 18 G Hepa-cut ($F = 11\%$), compared to the 21 G Biomol ($F = 42\%$) FNA needles (Student's t -test, $p < 0.01$).

Schulman et al. [28] found no difference in incidence of fragmentation in biopsies from human cadaveric liver tissue, when using 19 G SharkCore ($F = 16\%$), 22 G SharkCore ($F = 16\%$), 18 G QuickCore ($F = 16\%$), and 18 G Temno ($F = 23\%$) needles.

Complication Rate. The relation between needle gauge and incidence of pain or complications was analyzed in six studies. No relations were reported in five studies [15,21,22,24,25]. An increase in pain for larger diameter needles was reported in one study [26]. One study reported less pain when using CNB, compared to FNA needle types [18]. However, on average, more needle passes were required with the FNA needles. In a study including 6613 biopsies, major adverse events occurred in 0.7%

of biopsies ($n = 49$), including hematoma requiring transfusion and/or angiographic intervention ($n = 34$), infections ($n = 8$), and hemathorax ($n = 4$) [29]. Three patients (0.05%) died within 30 days of liver biopsy, one being directly related to biopsy.

Tublin et al. [25] compared postprocedure pain (10-point scale) at 1 h, 3 h, and 24 h, after use of 16 G and 18 G Max-Core CNB needles. Combined incidence of moderate or severe pain (score > 3) was 14.7% (1 h), 9.3% (3 h), and 6.7% (24 h), against 13.3% (1 h), 10.7% (3 h), and 9.3% (24 h). A linear relation between gauge and postbiopsy pain was not found (150 patients).

Vijayaraghavan et al. [24] presented postprocedure incidence of bleeding complications and moderate pain (score > 5, 10-point scale), after use of 18 G and 20 G Temno CNB needles. No effect of needle gauge was found on incidence of pain ($n = 11$, 1.5% and $n = 2$, 4.1%) and bleeding complications ($n = 6$, 0.8% and $n = 0$, 0%), respectively (Fisher's Exact Test, $p = 0.3$). Six cases of hemorrhage (0.8%) and one case of mortality (0.1%) were reported.

Chevallier et al. [22] presented pain scores on a visual analog scale (VAS, 0–100) immediately after (HI) and 6 h after (H6)

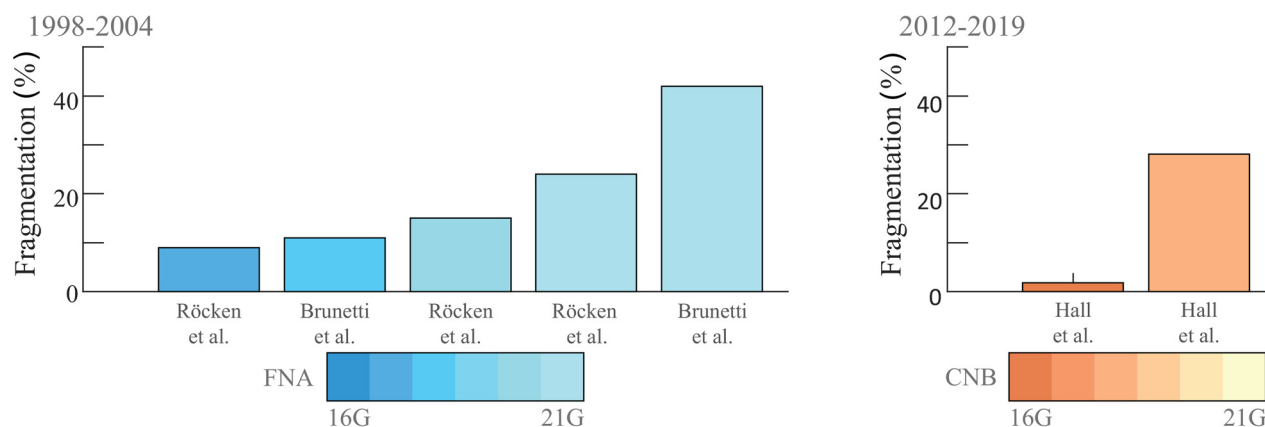


Fig. 5 Fragmentation of liver biopsies acquired with FNA or CNB needles, in the time periods 1998 and 2004 and 2012 and 2019. Face color intensities of bars indicate needle gauge (16–21 G).

procedures. Pain after use of 18 G Gallini CNB needles was 3.8 ± 11.0 (HI) and 2.7 ± 10.0 (H6) (not significant), respectively. Incidences of vasovagal reactions ($n=8$, 1.3%) and upper digestive hemorrhage ($n=1$, 0.2%) were reported.

Sparchez et al. [18] found a difference in incidence of pain at the moment of puncture, using 18 G FNA Surecut (58.2%) and 18 G CNB Biopsy Gun (29.5%) needles ($p < 0.05$, test not specified). The average number of passes was 1.6 and 1.3, respectively.

Three studies compared pain incidence of needles with a different gauge and brand. Li et al. [26] presented higher pain perception (VAS, undefined maximum) in patients treated with 18 G Tru-Cut CNB (1.2 ± 0.7), compared to 21 G Hakko FNA (0.3 ± 0.6) needles (Student's t -test, $p < 0.01$). Other incidences occurred with the 18 G Tru-Cut needles, including hemorrhages ($n=3$, 6.5%) and arteriovenous shunts ($n=4$, 8.7%). Hall et al. [15] used a prospective patient audit to quantify incidence of pain 2 h after procedures. No difference between 16 G Biopince ($n=13$, 48.2%) and 18 G Achieve ($n=6$, 42.9%) CNB needles was found ($p = ns$, Fisher's exact test) and no major complications were reported. Brunetti et al. [21] reported pain 4 h after procedures for 18 G Hepa-cut ($n=3$, 2%) and 21 G Biomol ($n=1$, 0.7%) FNA needles. For the 18 G needle, vasovagal reactions ($n=3$, 2%) were reported.

Discussion

Review Outcomes. The aim of this review was to evaluate the effect of needle gauge and type, on number of PTs, TCL, fragmentation, and complication rates, during acquisition of percutaneous ultrasound-guided liver biopsies. Our literature search provided a perplexing temporal division of data, with studies between 1998–2004 and 2012–2019, which was conserved in the visualization of results. Biopsy specimens were categorized as being adequate ($PT \geq 11$, $TCL \geq 20$ mm), compromised ($PT < 11$, $TCL < 20$ mm), or inadequate ($PT < 6$, $TCL < 15$ mm), according to AASLD recommendations. Adequate PT numbers were achieved with two passes of 16/17 G FNA needles, or with a single pass of 16/18 G CNB needles.

Specimen adequacy is determined by a sufficient number of complete portal tracts [2,10]. This is supported by a sufficiently large TCL, as parenchymal abnormalities are irregularly distributed [2]. With this in mind, none of the tested needle types between 1998 and 2004 resulted on average in adequate PT numbers, although TCL was adequate with 44% (4/9) of tested needle types. This is in line with the findings of Cholongitas et al. [10]. Between 2012 and 2019, TCL was adequate in 33% (2/6) and PT numbers in 83% (5/6) of tested conditions. This improvement in adequacy should significantly increase reliability of biopsy outcomes. However, ideally, specimen *means and their error bars* should exceed adequacy thresholds, i.e., reliable biopsy outcomes are desired for each patient. Presently, this is not yet the case.

An explanation of the increase in obtained number of complete portal tracts with similar reported TCL is currently missing in literature. This may partly result from an overall increase in used needle diameters (mean diameter was 19 G versus 17 G). Alternative explanations that could not be studied with available data include a reduction in fragmentation resulting in more complete portal tracts, biopsy device improvements, or thinner-walled needles.

The effect of increased needle diameter on TCL was positive in three studies (50%), negative in one study, and two studies found no effect. Increased diameter had a positive effect on obtained number of portal tracts in four out of four studies (100%), and a positive effect on reduced fragmentation in three out of four studies (75%). No relation between needle gauge and fragmentation was found in one study. No relation between needle gauge and complications or pain was found in five out of six studies (83%). Increased pain for larger diameter needles was found in one study.

Review Limitations. As a result of strict inclusion criteria, the number of articles suitable for this review was limited and meta-

analysis was not feasible. In addition, grouping of needles was complicated by technological progress, including the introduction of automated biopsy guns and new tip types. Furthermore, pain classification requires standardization. Pain was studied on 3-point scales [24], 10-point scales [25], 0–100 visual analog scales (VAS) [22], or directly by percentages [15]. It was measured before biopsies, immediately after biopsies, after 1 h, 2 h, 3 h, 6 h, or 24 h. Finally, statistical comparisons relied on grouping of scores, using arbitrary thresholds for mild, moderate, and severe pain. Interstudy comparison of results was impossible.

Finally, reported outcomes were affected by variables outside of the review scope. Vijayaraghavan et al. [24] showed that specimen TCL obtained with 1 or 2 passes was significantly larger compared to 3 or more passes. In addition, needle tip shapes may affect placement accuracy [30], and some CNB needles have centered instead of bevel tips (Fig. 2). Finally, type and experience of operators [19,22,27], as well as included hepatic diseases and severity [10,19], can affect biopsy adequacy.

Conclusions

Liver biopsy adequacy of mean reported number of portal tracts ($PT \geq 11$) has increased from 0% (1998–2004) to 83% (2012–2019). This should have significantly increased reliability of biopsy outcomes. With current devices, adequate PT numbers were achieved with 16/17 G FNA Menghini-modified (two passes) or 16/18 G CNB (one pass) needles. Overall, an increase in needle diameter positively affected TCL (in 50% of studies), number of portal tracts (100%) and reduced fragmentation (75%). Effects of needle diameter on perceived pain and complications were found insignificant (83%). However, complication rates were low in general and statistical testing requires larger sample sizes. Ideally, specimen *means and their error bars* should exceed adequacy thresholds, i.e., reliable biopsy outcomes are desired for each patient. This stresses the need for additional research and development in the fields of needle design, utilization, training, and histological analysis of specimens.

Nomenclature

CNB = core needle biopsy
EUS = endoscopic ultrasound
FNA = fine needle aspiration
TCL = total core length
VAS = visual analog scale

Funding Data

- Dutch Research Council (NWO, Project No. 16932).

References

- [1] Campbell, M., and R. Reddy, K., 2004, "The Evolving Role of Liver Biopsy," *Aliment Pharm. Ther.*, **20**(3), pp. 249–259.
- [2] Rockey, D. C., Caldwell, S. H., Goodman, Z. D., Nelson, R. C., and Smith, A. D., 2009, "Liver Biopsy," *Hepatology*, **49**(3), pp. 1017–1044.
- [3] Pineda, J. J., Diehl, D. L., Miao, C. L., Johal, A. S., Khara, H. S., Bhanushali, A., and Chen, E. Z., 2016, "EUS-Guided Liver Biopsy Provides Diagnostic Samples Comparable With Those Via the Percutaneous or Transjugular Route," *Gastrointest. Endosc.*, **83**(2), pp. 360–365.
- [4] Lefkowitz, J. H., 2015, *Scheuer's Liver Biopsy Interpretation E-Book*, Elsevier Health Sciences, Edinburgh, UK.
- [5] Mani, H., and Kleiner, D. E., 2009, "Liver Biopsy Findings in Chronic Hepatitis B," *Hepatology*, **49**(S5), pp. S61–S71.
- [6] Brunt, E. M., 2001, "Nonalcoholic Steatohepatitis: Definition and Pathology," *Semin. Liver Dis.*, **21**(1), pp. 3–16.
- [7] Colloredo, G., Guido, M., Sonzogni, A., and Leandro, G., 2003, "Impact of Liver Biopsy Size on Histological Evaluation of Chronic Viral Hepatitis: The Smaller the Sample, the Milder the Disease," *J. Hepatol.*, **39**(2), pp. 239–244.
- [8] Gor, N., Salem, S. B., Jakate, S., Patel, R., Shah, N., and Patil, A., 2014, "Histological Adequacy of EUS-Guided Liver Biopsy When Using a 19-Gauge non-Tru-Cut FNA Needle," *Gastrointest. Endosc.*, **79**(1), pp. 170–172.
- [9] Bravo, A. A., Sheth, S. G., and Chopra, S., 2001, "Liver Biopsy," *New Engl. J. Med.*, **344**(7), pp. 495–500.

- [10] Cholongitas, E., Senzolo, M., Standish, R., Marelli, L., Quaglia, A., Patch, D., Dhillon, A. P., and Burroughs, A. K., 2006, "A Systematic Review of the Quality of Liver Biopsy Specimens," *Am. J. Clin. Pathol.*, **125**(5), pp. 710–721.
- [11] Pritzker, K. P. H., and Nieminen, H. J., 2019, "Needle Biopsy Adequacy in the Era of Precision Medicine and Value-Based Health Care," *Arch. Pathol. Lab. Med.*, **143**(11), pp. 1399–1415.
- [12] Bedossa, P., Dargere, D., and Paradis, V., 2003, "Sampling Variability of Liver Fibrosis in Chronic Hepatitis C," *Hepatology*, **38**(6), pp. 1449–1457.
- [13] DeWitt, J., McGreevy, K., Cummings, O., Sherman, S., LeBlanc, J. K., McHenry, L., Al-Haddad, M., and Chalasani, N., 2009, "Initial Experience With EUS-Guided Tru-Cut Biopsy of Benign Liver Disease," *Gastrointest. Endosc.*, **69**(3), pp. 535–542.
- [14] Gleeson, F. C., Clayton, A. C., Zhang, L., Clain, J. E., Gores, G. J., Rajan, E., Smyrk, T. C., Topazian, M. D., Wang, K. K., Wiersma, M. J., and Levy, M. J., 2008, "Adequacy of Endoscopic Ultrasound Core Needle Biopsy Specimen of Nonmalignant Hepatic Parenchymal Disease," *Clin. Gastroenterol. Hepatol.*, **6**(12), pp. 1437–1440.
- [15] Hall, T. C., Deakin, C., Atwal, G. S. S., and Singh, R. K., 2017, "Adequacy of Percutaneous Non-Targeted Liver Biopsy Under Real-Time Ultrasound Guidance When Comparing the Biopince (TM) and Achieve (TM) Biopsy Needle," *Br. J. Radiol.*, **90**(1080), p. 20170397.
- [16] Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., and Group, P., The PRISMA Group 2009, "Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement," *PLoS Med.*, **6**(7), p. e1000097.
- [17] Higgins, J. P., and Green, S., 2008, *Cochrane Handbook for Systematic Reviews of Interventions*, Wiley Online Library, Hoboken, NJ.
- [18] Sparchez, Z., Albu, S., Fayyad, E., Dumitra, D., Ban, A., and Pascu, O., 2000, "Comparison of Two Needles, the Surecut (18G) Versus the 'Biopty Gun' (Bard 18G) in Percutaneous Liver Biopsy," *J. Hepatol.*, **32**, pp. 182–182.
- [19] Röcken, C., Meier, H., Klauk, S., Wolff, S., Malferteiner, P., and Roessner, A., 2001, "Large-Needle Biopsy Versus Thin-Needle Biopsy in Diagnostic Pathology of Liver Diseases," *Liver*, **21**(6), pp. 391–397.
- [20] Siddique, I., Abu El-Naga, H., Madda, J. P., Memon, A., and Hasan, F., 2003, "Sampling Variability on Percutaneous Liver Biopsy in Patients With Chronic Hepatitis C Virus Infection," *Scand. J. Gastroenterol.*, **38**(4), pp. 427–432.
- [21] Brunetti, E., Silini, E., Pistorio, A., Cavallero, A., Marangio, A., Bruno, R., and Filice, C., 2004, "Coarse vs. Fine Needle Aspiration Biopsy for the Assessment of Diffuse Liver Disease From Hepatitis C Virus-Related Chronic Hepatitis," *J. Hepatol.*, **40**(3), pp. 501–506.
- [22] Chevallier, P., Ruitort, F., Denys, A., Staccini, P., Saint-Paul, M. C., Ouzan, D., Motamedi, J. P., Tran, A., Schnyder, P., and Bruneton, J. N., 2004, "Influence of Operator Experience on Performance of Ultrasound-Guided Percutaneous Liver Biopsy," *Eur. Radiol.*, **14**(11), pp. 2086–2091.
- [23] Sporea, I., Gherhardt, D., Popescu, A., Şirli, R., Cornianu, M., Herman, D., and Bota, S., 2012, "Does the Size of the Needle Influence the Number of Portal Tracts Obtained Through Percutaneous Liver Biopsy?," *Ann. Hepatol.*, **11**(5), pp. 691–695.
- [24] Vijayaraghavan, G. R., Vedantham, S., Rangan, V., Karam, A., Zheng, L., Roychowdhury, A., and Hussain, S., 2015, "Effect of Needle Gauge and Lobe Laterality on Parenchymal Liver Biopsy Outcome: A Retrospective Analysis," *Abdom. Imaging*, **40**(5), pp. 1223–1229.
- [25] Tublin, M. E., Blair, R., Martin, J., Malik, S., Ruppert, K., and Demetris, A., 2018, "Prospective Study of the Impact of Liver Biopsy Core Size on Specimen Adequacy and Procedural Complications," *Am. J. Roentgenol.*, **210**(1), pp. 183–188.
- [26] Li, G. P., Gong, G. Q., Wang, X. L., Chen, Y., Cheng, J. M., and Li, C. Y., 2013, "Fine Needle Aspirating and Cutting is Superior to Tru-Cut Core Are Needle in Liver Biopsy," *Hepatob. Pancreat. Dis.*, **12**(5), pp. 508–511.
- [27] Sporea, I., Popescu, A., Foça, M., Becheanu, G., Şirli, R., Cornianu, M., Gheorghie, L., Prelipcean, C., Mihai, C., Rogoveanu, I., and Săndulescu, L., 2013, "Do the Needle Type and the Operator Experience Influence Liver Biopsy Specimen Quality?," *Cent. Eur. J. Med.*, **8**(5), pp. 669–673.
- [28] Schulman, A. R., Thompson, C. C., Odze, R., Chan, W. W., and Ryou, M., 2017, "Optimizing EUS-Guided Liver Biopsy Sampling: Comprehensive Assessment of Needle Types and Tissue Acquisition Techniques," *Gastrointest. Endosc.*, **85**(2), pp. 419–426.
- [29] Boyum, J. H., Atwell, T. D., Schmit, G. D., Poterucha, J. J., Schleck, C. D., Harnsen, W. S., and Kamath, P. S., 2016, "Incidence and Risk Factors for Adverse Events Related to Image-Guided Liver Biopsy," *Mayo Clin. Proc.*, **91**(3), pp. 329–335.
- [30] van de Berg, N. J., de Jong, T. L., van Gerwen, D. J., Dankelman, J., and van den Dobbelsteen, J. J., 2017, "The Influence of Tip Shape on Bending Force During Needle Insertion," *Sci. Rep.*, **7**(1), p. 40477.