

How often do our liver core biopsies reach current definitions of adequacy?

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ABSTRACT

Needle core biopsy is a key tool in diagnosis and assessment of many medical liver diseases, but there is evidence that the combination of small size of the specimen obtained and the patchy nature of many of these diseases can result in misdiagnosis or incorrect staging. The Royal College of Pathologists has therefore published guidelines for assessment of adequacy. To assess whether these guidelines were being observed, we reviewed cases reported in our department over a 15-year period. Results showed that only 19.8% of cores would be considered adequate, 56.4% were suboptimal and 23.8% were inadequate. We discuss the issues around recommendations on the minimum size of liver biopsies, potential factors limiting biopsy size and whether further refinement of the guidelines for adequacy is required.

INTRODUCTION

Core biopsy remains an essential tool in diagnosis and staging of medical liver disease. However, only a tiny proportion of the liver is sampled and, as liver diseases may be patchy, there is potential for misdiagnosis due to sampling error. For example, fibrosis can be heterogeneously distributed,¹ and as a result, there is a bias in assessment towards lower degrees of fibrosis and inflammation in shorter biopsies.¹

To minimise this bias, various minimum biopsy sizes and portal tract numbers have been suggested: 10 mm,² 20 mm³ and 25 mm.¹⁻⁴ The Royal College of Pathologists (RCPath) has incorporated minimum adequacy requirements for staging in its document “*Tissue pathways for liver biopsies for the investigation of medical disease and for focal lesions*”⁵ as follows: ‘In general, a liver biopsy should be at least 1 cm long and contain a minimum of six portal tracts. The diameter of the core is also important and broader gauge needles are preferable for medical biopsies. Clinicians and pathologists should be aware that assessment of disease stage is compromised in biopsies less than 20 mm long, 1.4 mm wide, or containing fewer than 11 portal tracts, although this amount of tissue is not always available in practice.’

To assess the proportion of biopsies achieving these standards, a review of all liver biopsies for medical disease reported in our institution over a 15-year period was undertaken.

METHODS

All liver core biopsies reported in Oxford from January 1997 to December 2011 were identified from the histology reporting system FileMaker Pro using the search terms ‘liver biopsy’. All core

biopsies were taken by radiologists, although information on the level of experience of the radiologists (trainee vs Consultant) was not available. Mass lesion biopsies were excluded as were referrals. Cases were excluded if the report failed to include one or more of total core length, number of portal tracts and Ishak stage for fibrosis.

Total number of cores, length of longest core, total core length, numbers of portal tracts and central veins, Ishak fibrosis stage (in Oxford all our liver cores are discussed at a weekly clinicopathological correlation meeting and our hepatologists find it useful to have an Ishak staging score as shorthand for the degree of fibrosis in a biopsy, irrespective of the cause) and comments on adequacy were obtained from each report. Biopsy width was not available as it had not been included in reports, although biopsies had been performed according to standard protocols. Biopsies were grouped into three categories based on the RCPath guidelines (table 1).

All core lengths were assessed following fixation (ie, the measurement on the glass slide). For assessment of adequacy of core biopsy length, the total core length was used (the sum of the lengths of all fragments received).

In cases that would be considered inadequate using RCPath guidelines, the report archive was searched to determine if a repeat biopsy had been performed and at what time after the original biopsy.

RESULTS

One thousand three hundred forty-two of the 2796 medical liver biopsies contained the required information for inclusion. Of the excluded cases, 1022 (70.3%) included no length measurement, 152 (10.5%) no Ishak stage and 23 (1.6%) no portal tract count, while 257 (17.6%) reports were missing more than one of these. Patient demographics, average core biopsy length, number of portal tracts and portal tract: central vein ratio are shown in online supplementary table S1. No comparison of transjugular versus percutaneous biopsy

Table 1 Royal College of Pathologists definition of adequacy of liver core biopsies for medical disease

Category	Description
Inadequate	Less than 10 mm length and/or less than six portal tracts
Compromised	At least 10 mm length and six portal tracts but less than 20 mm and 11 portal tracts
Adequate	At least 20 mm length and 11 portal tracts

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could be made as the type of biopsy procedure was not stated on the majority of request forms.

Two hundred and sixty-six cores (19.8%) were considered adequate using the RCPATH guidance. Seven hundred and fifty-seven (56.4%) were above the minimum standard but of a size (length and number of portal tracts) at which assessment would be compromised and 319 (23.8%) were inadequate, being below the minimum length, minimum number of portal tracts or both. As the RCPATH guidance was only issued in 2008, numbers of adequate, compromised and inadequate core biopsies pre-2008 and post-2008 were also calculated (table 2). The increased proportion of adequate biopsies since introduction of the guidelines was statistically significant ($p < 0.011$ using $\chi^2 2 \times 3$ contingency table).

Only 40 of the 319 reports on inadequate cores (15%) commented on adequacy. The comments were largely that assessment of fibrosis and architecture was difficult on the limited material.

Only 2 (0.6%) of the inadequate biopsies were repeated within 3 months.

The Ishak stage of the core biopsies broken down by adequacy is shown in table 3. The Spearman rank correlation is 0.23, $p < 0.001$, indicating a weak positive correlation between adequacy of core biopsy and Ishak stage.

DISCUSSION

There is much debate on what constitutes an adequate liver biopsy. The RCPATH guideline is 20 mm in length with at least 11 portal tracts.⁵ The basis for the College guidance is unclear although two papers are referenced.¹⁻³ Colloredo *et al*³ demonstrated that shorter biopsies resulted in underestimation of stage and grade in chronic hepatitis and suggested 2 cm as the minimum length to obtain at least 11 portal tracts. They stated that lengths less than 2 cm could be acceptable if at least 11 portal tracts are present. Bedossa *et al*,¹ using virtual biopsy specimens of varying lengths, found 25 mm was necessary to accurately stage fibrosis in hepatitis C using the METAVIR system. Conversely, others have suggested that shorter lengths may be adequate. Schiano *et al* suggested 10 mm as the adequate length in hepatitis C.² No significant improvement in diagnostic accuracy was achieved with lengths over 10 mm, although interobserver variation did decrease. Whatever the size criterion for adequacy, our results, however, do indicate that a shorter core length and/or reduced number of portal tracts is associated with a lower Ishak stage, suggesting that shorter cores are associated with understaging, as also found by Colloredo *et al*.³

Further uncertainty arises since it is also unclear from the literature and from the RCPATH guidelines whether a single core biopsy of greater than the minimum length is required, or whether several smaller fragments with a total length greater than the minimum would be acceptable.

Although there is no uniform consensus on the required length of a liver biopsy, the objective of this study was to assess

Table 3 Ishak stage broken down by adequacy

Ishak stage	Number of cases in each category (% of total in adequacy category)		
	Inadequate	Compromised	Adequate
0	87 (27.1)	92 (12.1)	19 (7.3)
1	91 (28.3)	232 (30.5)	63 (24.1)
2	66 (20.6)	175 (23.0)	49 (18.8)
3	23 (7.2)	85 (11.2)	48 (18.4)
4	5 (1.6)	44 (5.8)	20 (7.7)
5	12 (3.7)	49 (6.4)	24 (9.2)
6	21 (6.5)	84 (11.0)	38 (14.6)
Unassessable	16 (5.0)	0	0

how well, or otherwise, liver biopsies performed in our institution conformed to the RCPATH guidelines. Extraordinarily, less than 20% of core biopsies over a 15-year period met this standard, with around 80% of biopsies compromised or inadequate. Similar results have been reported from elsewhere with a recent audit at Southampton University Hospitals revealing that over half (52%) contained only six portal tracts, although 88% had a length of 10 mm or more.⁶ Furthermore, a systematic review from the Royal Free Hospital, London of the quality of liver biopsies has found that specimens had an average length and number of portal tracts well below the published optimum standard (>20 mm in length, >10 portal tracts) in more than half of all cases.⁷ However, these findings contrast with an Italian study in which 99.3% of biopsies received over a 6-month period were 1.5 cm in length or greater.⁸

Whether 10, 20 or 25 mm is the correct length, or whether it is the number of portal tracts that is crucial, it seems extraordinary that so many years after needle biopsy of the liver became an established practice, there is still uncertainty on such a vital issue as minimum quantity needed to establish a diagnosis, grading and staging with certainty.

The above also raises the question of why operators fail to take an 'adequate' biopsy. The experience of the operator seems to influence this, as previous studies have found a significantly increased number of inadequate cores when the biopsy taker is inexperienced.⁷⁻¹⁰ Greater total length of biopsy can be achieved with multiple passes, but studies have shown that the complication rate increases with the number of passes.¹¹⁻¹² Interestingly, neither the major complication rate⁷⁻¹¹ nor adequacy of the specimen⁷ is influenced by the gauge of needle used. Another explanation may be that the clinician requesting or performing the biopsy is unaware of the need to achieve a minimum size and the implications of failing to do so.

As an alternative explanation, perhaps the view of clinicians and pathologists on adequacy of a particular biopsy varies depending on the clinical requirements, and therefore a biopsy that provides clinically useful information is regarded as acceptable whatever the length. Of the 40 cases in this study that were explicitly described as inadequate by the reporting pathologist, only two underwent a repeat biopsy within 3 months, suggesting that even an inadequate biopsy provides sufficient information to allow hepatologists to plan the next stage of management. In addition, diagnosis of medical liver disease is not dependent on core biopsy result alone. Serological, virological and biochemical results, radiological findings, including the results of endoscopic retrograde cholangiopancreatography and magnetic resonance cholangiopancreatography, and the clinical features all influence interpretation of liver core biopsies and subsequent clinical

Table 2 Comparison of adequacy preintroduction and postintroduction of RCPATH guidelines (percentages in brackets)

	Inadequate	Compromised	Adequate
Pre-2008	237 (24.5)	560 (58.0)	169 (17.5)
2008 onwards	82 (21.9)	201 (53.5)	93 (24.7)

management. Liver core biopsies have previously been considered essential for staging of liver diseases such as hepatitis C, and much of the argument on optimal core biopsy size centres around the minimum size to accurately assess fibrosis, but the advent of newer, non-invasive techniques such as fibroscanning should reduce the emphasis on core biopsy staging.

Potential limitations of this study include our lack of knowledge on the level of experience of the biopsy takers, the needle gauge of the biopsies and of the numbers of transjugular versus percutaneous biopsies. However, we feel that our study reflects practise in reality, where biopsies of difficult sizes are taken by different routes by a group of different individuals, strengthening our conclusions rather than weakening them.

CONCLUSION

Among liver pathologists there still seems to be emphasis on trying to define adequacy in liver core biopsies. However, it is clear from the literature that there is no uniformly agreed minimum standard for adequacy of the length of a liver biopsy, and this study has shown that current adequacy criteria for staging in the RCPATH guidelines are not being met in the majority of cases reported in our institution. Our study also reveals, however, that very few patients whose biopsies would be regarded as inadequate by these criteria are actually undergoing repeat biopsies.

There are three possible conclusions. First, if there truly is a minimum size below which an accurate report cannot be given, then this needs to be established and uniformly adopted. Pathologists should specifically detail in their report whether the

biopsy is adequate or not. Second, and conversely, if there is no such minimum size, then pathologists and clinicians should recognise and adopt this. Lastly, and our preferred conclusion is that, with the ready availability of virological, serological, biochemical and radiological testing, and particularly, with the development of non-invasive techniques to assess the degree of fibrosis, the size of the core biopsy is not crucial to clinical management. However, there are a small number of situations where the size of the biopsy does matter. Identifying such situations can only be the result of close clinicopathological correlation, which should, of course, be integral to all liver biopsy reporting.

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Contributors KF conceived the project. EPF collected and analysed the data and wrote the first draft. All authors contributed to the planning of the project and subsequent drafts of the paper.

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Take home messages

- ▶ Current adequacy criteria for disease staging are not being met in the majority of liver core biopsies reported at our institution.
- ▶ This has not, however, resulted in large numbers of repeat biopsies.
- ▶ We conclude that this either indicates a lack of awareness of adequacy criteria among pathologists and clinicians, or, more likely, that clinicians regard the results of liver biopsy as only one facet of their investigation, to be integrated with clinical and radiological findings.