

<sup>1</sup>Clinical Pharmacy, Maxima Medical Center,  
PO Box 7777, 5500 MB Veldhoven, The Netherlands,  
<sup>2</sup>Gastroenterology and Hepatology, Academic Hospital  
Maastricht, Maastricht, The Netherlands,  
<sup>3</sup>Gastroenterology and Hepatology,  
VU University Medical Center, Amsterdam,  
The Netherlands  
E-mail address: l.derijks@mmc.nl

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doi:10.1016/j.jhep.2005.11.049

## Length versus width in liver biopsies

*To the Editor:*

Assessing antiviral therapy in chronic viral hepatitis has renewed interest in liver biopsy (LB) quality, as changes in grading and staging after antiviral therapy are end points in most clinical studies [1]. Thus, where paired biopsies are necessary, optimal LB should be used. Recently, only LB samples 20–25 mm long have been considered adequate for assessment of grade and stage; these criteria have been rapidly adopted as optimal standards [2,3].

Apart from length, width and fragmentation also determine the quality of LB [4], but counting complete portal tracts (CP) has been considered a better parameter [4]. Colloredo et al. [2] concluded that “the critical factor influencing the negative effect of smaller sizes is probably the significant drop in number of CP in the smaller specimens.” In their study [2], as no percutaneous LB (PLB) with  $\leq 1$  mm width (assessed by masking with paper) contained  $\geq 11$  CP, regardless of length, they also stated that LB  $\leq 1$  mm width should be considered a priori, inadequate, irrespective of the LB length, i.e. a suboptimal biopsy.

We believe this stipulation regarding biopsy width [2] is an error. Considering that their paper has been adopted as a reference standard, it is particularly important to explore this. Colloredo et al. examined biopsies taken with 16 G Menghini needle. Its internal diameter is 1.4 mm. Therefore, 1.4 mm cannot be the standard width of biopsies, but only a potential maximum width. Secondly, due to fixation, shrinkage will occur. Thirdly, a microtome cutting plane could never always cut through the maximum diameter of the biopsy cylinder when making sections—a range of widths would be

expected. Fourthly, and more importantly, previous literature has shown smaller average widths of biopsies for equivalent or larger size needles. With a larger 14 G needle [5], which has an internal diameter of 1.6 mm, the average biopsy core width was only  $0.9 \pm 0.3$  (SD) mm. This average is only two thirds of the 1.4 mm width reported by Colloredo et al. Moreover, the 2 SD reported [5] means the upper cut off is 1.5 mm width, i.e. only 5% of specimens were above this. Even if 20% were 1.4 mm or more (the uniform width stated in Colloredo's paper) this does not approach the universal 1.4 mm width reported by Colloredo et al. (who made no selection based on width). Moreover, with the biopsy widths described by Crawford et al. [5], 6 CP/1 cm were observed using a 14 G needle—which is almost the same as the 11 or more CP seen in 2 cm length biopsies reported by Colloredo et al. [2]. This again imputes an error in the widths reported by Colloredo et al. [2] as the CP count is similar, taking into account increased length.

Menghini, in his original paper [6], also has an average LB width of 0.75 mm, which is only just over half that described by Colloredo et al. [2], with a larger 1.5 mm inner core needle (15 G). Thus, two previous papers show that biopsy widths with larger needles than 16 G, give a far reduced average width than that given by Colloredo et al. [2]. We believe the way the data analysis is described, implies that the biopsies were assumed to be the diameter of the inner core of a 16 G needle, rather than measured directly, and appropriate calculations were probably made on this premise.

Recently, we evaluated 312 consecutive real transjugular liver biopsies (TJLB) using 19 G Tru-cut needle [7].

We were precise in defining portal tracts using the definitions by Crawford et al. [5]. Although the median TJLB width was 0.6 mm (range 0.5–0.8), we found a median length and CP of 22 mm and 8, respectively. Moreover, 50 (26%) TJLB had  $\geq 11$  CP. Thus, despite a narrower biopsy  $< 1$  mm, 11 CP or more (the gold standard, which we agree should be adopted), were seen; this manifestly contradicts the statement that  $< 1$  mm biopsies should be considered inadequate [2], as some reach optimal standards.

Another consequence of setting new standards for the quality of LB is the following important question for clinical practice. How can an optimal LB be obtained routinely? In our systematic review of PLB [8] the mean CP was suboptimal ( $7.5 \pm 3.4$ ). Moreover, Colloredo et al. [2] selected 161 PLB from 355 biopsies, based on length  $> 3$  cm, not width, i.e. 55% were considered inadequate. This means that using a standard percutaneous approach, more than one pass would be needed to obtain sufficient tissue—this is known to increase complications [8]. Our data with TJLB, given that multiple passes have not increased complications [9,10], suggests that TJLB with sufficient passes could be an alternative and safe approach to obtain an optimal LB, particularly in clinical trials, despite the average width of biopsies being  $\leq 1$  mm.

Evangelos Cholongitas<sup>1</sup>, Alberto Quaglia<sup>2</sup>,  
Amar P. Dhillon<sup>2</sup>, David Patch<sup>1</sup>,  
Andrew Kenneth Burroughs<sup>1</sup>

<sup>1</sup>Liver Transplantation and Hepatobiliary Medicine,  
Royal Free Hospital, Pond Street, Hampstead,  
London NW3 2QG, UK,

<sup>2</sup>Histopathology Department, Royal Free Hospital,

Pond Street, Hampstead, London NW3 2QG, UK  
E-mail address: andrew.burroughs@royalfree.nhs.uk

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doi:10.1016/j.jhep.2005.12.023

## Clinical practice and ideal liver biopsy sampling standards: Not just a matter of centimeters

*To the Editor:*

The letter by Dr Cholongitas et al. raises crucial issues and warrants both ‘technical’ comments and clinical considerations.

Concerning the technical points, even after carefully re-reading our manuscript [1], we were unable to find the sentence that Dr Cholongitas mentions: “no percutaneous liver biopsy with  $\leq 1$  mm width contained  $\geq 11$  complete portal tracts (CPT) regardless of the length”. Table 3 of the paper clearly shows that biopsy samples  $\geq 3$  cm long/1 mm width contained  $11.2 \pm 2.4$  CPT. Indeed, we found  $\geq 11$  CPT in 104 out of 161 (64.6%) liver biopsies  $\geq 3$  cm long/1 mm, but the grading and staging of these samples was significantly milder compared to those  $\geq 3$  cm long/1.4 mm wide (as shown in Table 3).

As for the relationship between the internal diameter of the needle and the diameter of the core biopsy, it is self-evident that they cannot coincide: because of shrinkage, the fixation results

in the reduction of the biopsy diameter and (obviously) in a reduced size of the portal tracts. It is less believable, however, that originally complete portal triads become incomplete! Different core biopsy sizes reported in different studies may well be due to technical variables (i.e. type, duration, and temperature of fixation, technical skill embedding and cutting samples) or to structural features of the needles.

Finally, Dr Cholongitas et al. rightly remind us that 194 of our original series of 355 biopsies were not included in the study, inferring that they were ‘inadequate’: among the samples that we excluded, 142 (73%) were between 2 and 2.9 cm long and would have been considered ‘adequate’ even in the light of the outcome of our study.

To avoid boring pathologists and clinicians alike with a sterile dispute on millimeters, we would rather emphasize the main message of our paper: our ‘experimental’ model [1], like other similar studies [2,3], demonstrated that a liver biopsy sample 1.5 cm long and/or thinner than 1 mm carries a