



## Transjugular liver biopsy: how good it is for accurate histological interpretation?

Evangelos Cholongitas, Alberto Quaglia, Dimitrios Samonakis, Marco Senzolo, Christos Triantos, David Patch, Gioacchino Leandro, Amar Dhillon and Andrew Kenneth Burroughs

*Gut* published online 24 Apr 2006;  
doi:10.1136/gut.2005.090415

---

Updated information and services can be found at:

<http://gut.bmjournals.com/cgi/content/abstract/gut.2005.090415v1>

---

*These include:*

**Email alerting service**

Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

---

### Notes

---

**Online First** contains unedited articles in manuscript form that have been peer reviewed and accepted for publication but have not yet appeared in the paper journal (edited, typeset versions may be posted when available prior to final publication). Online First articles are citable and establish publication priority; they are indexed by PubMed from initial publication. Citations to Online First articles must include the digital object identifier (DOIs) and date of initial publication.

---

To order reprints of this article go to:  
<http://www.bmjournals.com/cgi/reprintform>

To subscribe to *Gut* go to:  
<http://www.bmjournals.com/subscriptions/>

## Transjugular Liver Biopsy: How Good It Is for Accurate Histological Interpretation?

Evangelos Cholongitas<sup>1</sup>, Alberto Quaglia<sup>2</sup>, Dimitrios Samonakis<sup>1</sup>, Marco Senzolo<sup>1</sup>, Christos Triantos<sup>1</sup>, David Patch<sup>1</sup>, Gioacchino Leandro<sup>1</sup>, Amar P. Dhillon<sup>2</sup>, Andrew Kenneth Burroughs<sup>1</sup>

<sup>1</sup> Liver Transplantation and Hepatobiliary Medicine, Royal Free Hospital,

<sup>2</sup> Histopathology Department, Royal Free Hospital,  
Pond Street, Hampstead, London NW3 2QG, UK

### **Correspondence**

Corresponding Author: Andrew K. Burroughs, FRCP, Professor of Hepatology

Correspondence Address: Liver Transplantation and Hepatobiliary Medicine,  
Royal Free Hospital, Pond Street, Hampstead,  
London NW3 2QG, UK.

Email address: Andrew.Burroughs@royalfree.nhs.uk

**Key words:** liver biopsy, transjugular liver biopsy, Tru cut needle, sample size, portal tract

**Abbreviations:** LB: liver biopsy, PLB: percutaneous liver biopsy,  
TJLB: Transjugular liver biopsy, CP: complete portal tracts, LT: liver transplant, PPT: partial portal tracts

**ABSTRACT**

**Background:** Transjugular liver biopsy (TJLB) is often smaller and/or more fragmented than percutaneous liver biopsy (PLB). Recently, for PLB, the minimum requirements to evaluate chronic hepatitis have been set at  $\geq 20$ -25 mm length and  $\geq 11$  complete portal tracts (CP).

**Aim:** To evaluate and compare TJLB and PLB length, portal tract number, fragmentation and adequacy for histopathological diagnosis and staging.

**Patients/methods:** 326 consecutive TJLB in 274 patients (109 transplanted), always using 3 passes (19G Trucut) and 40 consecutive PLB (15G Menghini).

**Results:** No technical failures occurred with the TJLB, and histological diagnosis was possible in 98.5%. The median number of fragments was 5 (1-13), and the median total length was 22 mm (3-46), with 65%  $\geq 20$  mm and 36%  $\geq 25$  mm; 60% of TJLB  $\geq 28$  mm long had  $\geq 11$  CP. No difference in CP number or biopsy length was found between PLB and TJLB specimens.

**Conclusion:** TJLB with 3 passes is adequate for histological diagnosis with 89% being either  $\geq 15$  mm in length or having  $\geq 6$  CP. Although adequate sampling remains a limitation for staging and grading of chronic hepatitis, TJLB is comparable to PLB in this respect.

## INTRODUCTION

Liver biopsy (LB) is the "gold standard" for histological confirmation, diagnosis and severity of liver disease.[1][2]

Percutaneous (PLB) and transjugular (TJLB) liver biopsy are most frequently used.[1] [3][4][5][6][7] PLB is usually used first,[8][9] and TJLB used if there are contraindications such as significant coagulopathy or moderate ascites.[7] [10][11][12] However, TJLB is considered less satisfactory than PLB because smaller, more fragmented and thinner samples are obtained more frequently.[1] [10]

LB specimens represent approximately 1/50.000 of the liver.[10] Several studies have evaluated the minimum length and number of portal tracts necessary for optimal histological evaluation. Diagnostically, PLB of  $\geq 15$  mm length has been considered necessary for accurate diagnosis in chronic liver disease[13]; a review,[10] also concluded that 6 to 8 complete portal tracts (CP) should be present for diagnosis, most histopathologists accepting 6 portal tracts. However, with the increasing need to assess fibrosis in chronic hepatitis C and non-alcoholic fatty liver disease, 20-25 mm length and/or  $\geq 11$  CP have been considered necessary to reliably assess grading and staging and to reduce sampling errors.[14][15]

However, TJLB has received less attention with evaluation of only small cohorts.[16][17][18][19][20] Our aim was to evaluate length, fragmentation and number of portal tracts in a large TJLB series and to audit sample adequacy in relation to recently proposed standards for diagnosis and grading and staging.[14][15]

## MATERIAL AND METHODS

We evaluated 326 consecutive TJLB in 274 patients between January 2003 and May 2004. The main indications for TJLB were: a) prothrombin time  $\geq 5$  sec from control and/or platelet count less than  $50.000/\text{mm}^3$ , b) gross ascites, small cirrhotic liver or severe obesity and c) for liver transplant (LT) patients, a protocol liver biopsy or differential diagnosis of abnormal liver function tests, when either coagulopathy, cardiovascular compromise or patient co-operation might jeopardise the safe undertaking of a PLB.

We collected routine demographic, clinical and laboratory data. TJLB were performed in the interventional radiology suite following written consent with continuous electrocardiographic and oxygen saturation monitoring. The right internal jugular vein was punctured under ultrasound guidance following local anaesthesia. A guide wire followed by a sheath were introduced into the inferior vena cava and then, using a Cobra catheter, to the hepatic veins under fluoroscopic control. Hepatic venography was performed to evaluate hepatic vein anatomy. The needle was inserted toward the liver via a 5.0 F catheter and a sample obtained by passing the needle through the hepatic vein wall. All procedures were performed by an experienced radiologist or hepatologist using a 19G [Cook (Sandet 6, DK-4632 Bjaeverskov) or Kimal (Middlesex, UB8 2SA, England)] Tru-cut type biopsy needle (maximum core length 15-20 mm and external diameter 1 mm). Three passes were performed, our standard procedure since January 2003, regardless of size and adequacy of each core from each pass. Following this, a small amount of contrast media was injected to check for capsular puncture. TJLB was considered technically unsuccessful if it was impossible to obtain a liver

sample for any reason. Major complications (i.e. supraventricular tachycardia, capsular perforation or intra-peritoneal haemorrhage) were always recorded. Day cases were followed up in hospital for up to 6 hours, and 24 hours if an inpatient. Formal reporting by patients of any subsequent problems was evaluated from their discharge information sheet. Patients were seen within 2 weeks to discuss biopsy results.

We also evaluated 40 consecutive PLB in non-cirrhotic patients with abnormal liver function tests performed using a 15G Menghini needle as a comparison group. All TJLB and PLB were formalin-fixed and embedded in a paraffin wax block. Serial sections, 5  $\mu\text{m}$  thick, were cut and stained with haematoxylin and eosin (H&E), reticulin, Victoria blue, Masson Trichrome and Perls' method for iron. The pathologists (AD and AQ) initially reviewed biopsy sections without the clinical information. The number and length of each fragment (cores which were completely separated) were recorded. The length (mm) was measured with a ruler. The width (mm) was evaluated in a random cohort of 40 TJLB using measurement under the microscope recording the maximum diameter found. The total length was given by adding the fragment lengths. A sample was "too fragmented" when the histopathologists decided that the fragment number and size did not permit histological interpretation.

The portal tracts in each fragment on H&E sections were counted both as CP and as partial portal tracts (PPT) as defined by Crawford et al.,[21] i.e. "focus of connective tissue containing at least two luminal structures". A portal tract was considered complete when its full circumference was visible, or when at least three quarters of the circumference and three luminal structures (i.e. portal vein, hepatic artery and bile duct) were visible. A portal tract was considered partial when its circumference was incomplete and contained any two luminal structures. Foci with only one luminal structure were not counted as portal tracts. A single portal tract and its branches cut on a tangential plane can appear as multiple adjacent portal tracts. In this instance we regarded these structures as part of a single portal tract, when in the projection trajectory of the ramification of a dominant portal tract with little interposed parenchyma. When relatively large portal tracts (i.e. containing septal bile ducts ( $>100\mu\text{m}$ ) or medium sized (40-100  $\mu\text{m}$ ) interlobular bile ducts[22] were seen, complete portal tracts were defined only if all three portal structures were visible, and partial portal tracts only if two structures were present. Connective tissue cut longitudinally, along side the biopsy edges or large areas of connective tissue attached to the end of the biopsy core and containing only one vein, artery or bile duct were not considered as portal tracts. Portal tracts were not counted in TJLB which had severe architectural distortion (i.e. cirrhosis, advanced fibrosis and massive necrosis), because one cannot reliably recognize, separate and count individual portal tracts, in keeping with previous publication evaluating portal tract number.[23] This is because with severe fibrosis and cirrhosis, fibrous bridging is accompanied by loss of the portal tract boundaries, abnormal vascularisation, bile duct loss and ductular reaction resulting in complete effacement of the lobular architecture. The total number of CP or PPT was the summation of CP or PPT respectively, in each fragment. The total portal tract number was the summation of total CP and PPT.

To evaluate fragmentation in reducing the CP number, we evaluated the PPT at each end of each fragment (and not at its sides), considering them to

be contiguous when there were more than 3 fragments (each representing 1 pass of the 3 performed at each biopsy) and thus representing the maximum theoretical number of CP.

### Statistical analysis

All data were analyzed using the statistical package SPSS (version 10.0). The chi-square test was used for comparing qualitative variables and t-test and Mann-Whitney test for comparing quantitative variables. Quantitative variables normally distributed were expressed as mean values  $\pm$  one standard deviation (S.D.) and non-normally distributed as median values (range). Significance testing was two-sided and set to  $<0.05$ . The correlation between total length and total number of complete portal tracts in each TJLB and each fragment (i.e. as a separate liver biopsy) was evaluated by Spearman correlation. Comparisons were made between cirrhotic and non-cirrhotic biopsies, non-transplant versus transplant biopsies and between biopsies performed for grading and staging (known chronic hepatitis C, alcohol/NASH pre-transplant) and others performed for diagnostic reasons, and those performed for both diagnosis and staging/grading.

## RESULTS

**Patient characteristics.** The 274 patients had a median age of 51 (13-87) years and 174 (63.5%) were men; 165 were non-LT patients, each underwent only one TJLB. In the 109 LT patients 16 had 2 TJLB, 10 had 3, 4 had 4 and 1 had 5) (Table 1).

**Table 1:** Demographic and clinical characteristics of the 274 patients, who underwent Transjugular Liver Biopsy (TJLB).

Patients characteristic	non-LT (n=165)	LT (n=109)
Age (years)	48 $\pm$ 15	52 $\pm$ 9 <sup>§</sup>
Sex (male/female)	92/73	82/27 <sup>¶</sup>
Cause of underlying disease*, n (%)		
Primary Liver Disease	126 (77)	109 (100)
HCV	21 (13)	42 (39)
Alcohol/NASH	48 (29)	24 (22)
PBC/PSC	-	15 (14)
Autoimmune	13 (8)	4 (3)
Cryptogenic	31 (19)	16 (15)
Other <sup>†</sup>	13 (8)	8 (7)
Haematological disease <sup>‡</sup> , n (%)	25 (15)	-
Other/Unknown	14 (8)	-

PBC: Primary Biliary Cirrhosis, PSC: Primary Sclerosing Cholangitis, LT: liver transplant

\*For LT patients is the indication for liver transplantation

†Other: drug-induced hepatitis, haemochromatosis, Wilson's disease

‡Haematological disease: Lymphoma, Leukaemia, Graft Versus Host Disease

§: p=0.01

¶: p=0.001

In non-LT patients, 126 (77%) had suspected primary liver disease and 25 (15%) had underlying haematological disease. There were 70 (42%) cirrhotic and 95 (58%) non-cirrhotic patients. Diagnoses: 48 of 126 (29%) had alcoholic liver disease/NASH; other diagnoses are shown in Table 1. HCV related cirrhosis was the major indication for LT in 42 (38.5%), followed by ALD/NASH in 24 (22%) and PBC/PSC in 15 (14%) (Table 1).

**TJLB characteristics.** No TJLB failed to obtain liver samples, using three passes. The specimen was adequate for histological diagnosis in all but 5 (1.5%): 3 were too small and 2 were too fragmented. There were no major complications.

**Evaluation of fragmentation, length, width and portal tracts and comparison with PLB.** The median total length was 22 mm (range 3-46) with a median of 5 fragments (range 1-13); 290 TJLB (89%) were  $\geq 15$  mm long, 213 (65%)  $\geq 20$  mm, and 116 (36%)  $\geq 25$  mm. There was no significant difference in total length between cirrhotics and non-cirrhotics (23 vs 22 mm,  $p=0.07$ ) nor in the median number of fragments (4 vs 5,  $p=0.08$ ). There was also no significant difference in length between non-LT and LT biopsies (23 vs 22 mm,  $p=0.45$ ). Non transplant biopsies had less fragments, than transplant ones (4 vs 5,  $p=0.035$ ) (Table 2). The maximum width was a median of 0.6 mm (range 0.5-0.8).

**Table 2:** Characteristics of the 326 Transjugular Liver Biopsies (TJLB).

TJLB characteristic	Non-LT TJLB (n=165)	LT TJLB (n=161)	p
Inadequate sample, n	2	3	NS
Total length (median, mm)	23 (4-44)	22 (3-46)	NS
Number of fragments (median)	4 (1-11)	5 (1-13)	0.035
Number of complete portal tracts (median)*	8.5 (1-26)	8 (0-24)	NS
Number of partial portal tracts (median)*	6 (0-16)	5 (0-14)	NS
No portal tract evaluation, n (%)	97 (59)	35 (22)	<0.001
Cirrhosis, n (%)	70 (42)	15 (9)	<0.001
Total length $>15$ mm, n (%)	146 (88)	144 (89)	NS

LT: liver transplant, NS: no significant

\* in 194 transjugular liver biopsies in which portal tracts were counted

In 132 TJLB (58% non-LT / 22% LT,  $p<0.001$ ), 40% of the total, portal tracts were not counted because of: cirrhosis (85 - 64.4%), severe fibrosis (20 - 15.1%), severe infarction/necrosis (18 - 13.6%), ductopenia (7 - 5.2%) and excessive fragmentation (2 - 1.5%) cases (Table 2). Thus, portal tracts were counted in 194 TJLB: median total portal tracts (CP plus PPT) was 13 (range 2-38); median total number of CP was 8 (range 0-26) and PPT was 5 (range 0-16). The median CP:PPT ratio was 1.6 (range 0-12).

The median length and CP in the biopsies performed for diagnostic purposes ( $n=202$ ), or solely staging/grading ( $n=124$ ) or for both ( $n=137$ ) were respectively: for length 22 mm (3-46), 22 mm (9-44) and 22 mm (9-44) and for CP 8 (0-26), 8 (3-25) and 8 (3-25). TJLB  $\geq 15$  mm were 89%, 88% and 87% in the 3 groups, respectively, and those  $\geq 25$  mm were 34%, 38% and 38% in the 3 groups, respectively. TJLB with  $\geq 6$  CP were 73%, 82% and 80% in the 3 groups, respectively, and those with  $\geq 11$  CP were 26%, 24% and 24% in the 3

groups, respectively. There were no significant differences. There were also no differences when solely considering TJLB for chronic hepatitis C, in which median length was 22 mm (10-41) and CP was 8 (3-25) versus all the other biopsies, in which median length was 22 mm (3-46) and CP 8 (0-26). In the chronic hepatitis C biopsies 88.5% were  $\geq 15$  mm and 38% were  $\geq 25$  mm long.

In 76% of 194 TJLB there were  $\geq 6$  CP; these biopsies were significantly longer, than those with  $< 6$  CP (median length 22 mm vs 15 mm,  $p < 0.001$ ). In addition, TJLB with  $\geq 11$  CP (26%) were significantly longer, than those with  $< 11$  CP (median length 28 mm vs 20 mm,  $p < 0.001$ ). Although all TJLB with  $\geq 11$  CP were longer than 15 mm, only 50% of TJLB with  $\geq 25$  mm length had  $\geq 11$  CP. Finally, there was no significant difference between non-LT and LT TJLB regarding number of CP (8.5 vs 8,  $p = 0.19$ ) and PPT (6 vs 5,  $p = 0.17$ ) (Table 2).

In the PLB, the median total length and number of CP were 17 mm (range 5-49) and 7 (range 0-18), respectively, which were not significantly different compared to TJLB [median length 22 mm (range 3-46) and median CP 8 (0-26),  $p = 0.35$ ].

**Correlation between the length and CP in TJLB.** This was assessed in the 194 TJLB cohort (Spearman  $r = 0.49$ ,  $p < 0.001$ ) (Figure 1). A TJLB  $\geq 28$  mm long contained  $\geq 11$  CP in 60% versus 16% when  $< 28$  mm ( $p < 0.001$ ) (Figure 1).

In the 194 TJLB, 1045 fragments were obtained (Figure 2). The distribution of fragment length was similar to the entire TJLB cohort. Generally, longer fragments contained more CP (Figure 2); 212 (76.5%) of 277 fragments 1 mm long had no CP, and the remainder had 2 or 3 CP (Figure 2). Considering the 1045 fragments as separate liver specimens, there was good correlation between fragment length and CP ( $r = 0.72$ ,  $p < 0.001$ ). From this data, one can estimate that on average a non-fragmented specimen of  $\geq 23$  mm length would be needed to obtain the optimal number of 11 CP, i.e. the partial portal tracts at the ends (but not the sides) of all fragments but 3, would be considered to be contiguous, assuming each pass would obtain one unfragmented core. Thus, both an increase in length and reducing fragmentation of TJLB are required to improve the number of adequate liver biopsy specimens.

## DISCUSSION

Liver biopsy is an essential diagnostic tool in acute or chronic liver disease and in particular to estimate grading / staging.[1] [10] Adequate specimen size is crucial for accurate histological interpretation and elimination of sampling error and intra/inter observer variability,[24][25] but LB may still be suboptimal.[14][15] [26] Apart from length, width and fragmentation also determine the quality of LB. For this reason, counting complete portal tracts has been considered a better and more appropriate parameter for evaluation of a liver biopsy adequacy, and, thus, is the most suitable parameter to compare different kinds of liver biopsies (e.g percutaneous vs transjugular or Menghini vs Trucut or using different needle size) rather than solely liver biopsy length or width.[10] [15]. Liver biopsies with at least 6 CP are considered adequate for diagnosis of diffuse liver disease.[10]

Assessing antiviral therapy has renewed interest in LB quality. Changes in inflammation (grading) and fibrosis (staging) after antiviral therapy represent end points in most clinical trials. Recent studies[14][15] estimated that grade and stage were adequately assessed, only in samples 20-25 mm long and/or containing  $\geq 11$  CP. According to these criteria, both PLB and TJLB usually provide inadequate specimens: using 17G Menghini needle, only 42% of PLB had  $\geq 10$  CP,[23] and in the largest PLB series 45% were  $< 20$  mm long.[27] In our study, 37.1% of TJLB contained  $\geq 10$  CP and only 26%  $\geq 11$  CP. Using 3 passes, the median CP was 8. From the correlation (Figure 1) a median number of 11 CP could be achieved performing more than 3 passes, as TJLB  $\geq 28$  mm have  $\geq 11$  CP in 60%.

TJLB has often been considered suboptimal due to a higher frequency of inadequate specimens, related to the initial aspiration technique yielding small specimens, which too frequently were excessively fragmented.[28][29] The development of Tru-cut TJLB has improved quality without any increase in complications.[19] [30] Despite this, the perception of being a second class biopsy persists, and is reinforced further, considering current 'optimal' PLB criteria.[14][15] However, TJLB has some intrinsic characteristics that paradoxically could make it a more appropriate technique of liver biopsy, obtaining optimal specimens even with the current 'standards'. Multiple cores can be obtained, in contrast to PLB where more than one pass gives rise to increased complications.[6] [12] [31] Providing the liver capsule is not punctured with TJLB (does not occur with experienced operators), complications do not increase with multiple passes.[17] [26] [31][32][33] Minor complications such as neck pain are also infrequent as previously audited by our group.[33] However, the diameter of the TJLB needle is usually smaller than PLB, and fragmentation is also felt to be worse.[10]

Only 11 studies have evaluated Tru-cut TJLB in terms of type of needle, number of passes, length, fragmentation and portal tracts number (Table 3).[16][17][18][19] [34][35][36][37][38][39][40] In these studies, an average of 2.7 passes/ patient yielded specimens of  $14 \pm 2.6$  mm mean length and a mean number of  $6.4 \pm 2.3$  CP (Table 3). Only 3 studies included 100 TJLB or more; one reported results using a 1.2 mm diameter needle (number of passes not recorded), the mean length was  $16.5 \pm 6.1$  mm;[37] the second study reported a mean number of 5.6 portal tracts in 123 TJLB[38] and the last study evaluated 193 TJLB, which had a mean length of 18 mm.[19] In the last 2 studies needle diameter and number of passes are not given. In addition, only one study documented the number of fragments (mean=2.5), but the number of passes is not given.[17]

**Table 3.** Systematic review of 11 series of TJLB using Tru-cut needle and in which at least one of the following characteristics was documented: length, number of portals tracts, passes or fragments of liver biopsy tissue

Study	TJLB, n	Needle (G)	Pass, n	Fragment, n	Length, mm (mean)	PT, n (mean)
Kardache <sup>(16)</sup>	29	18	1	-	12	≥8*
De Hoyos <sup>(17)</sup>	52	18	-	2.5	17	6.2
Bruzzi <sup>(18)</sup>	50	18	2.2	-	1-20 <sup>†</sup>	10.4
Bull et al <sup>(19)</sup>	193	-	-	-	18	-
Choo <sup>(34)</sup>	7	18	2.9	-	12	-
Dimichele <sup>(35)</sup>	13	19	>3-5	-	13.6	6
Chau <sup>(36)</sup>	18	18	1-3	-	10	4
Elshakawy <sup>‡</sup> <sup>(37)</sup>	100	-	-	-	16	-
Regan <sup>(38)</sup>	123	-	-	-	-	5.6
Little et al <sup>(39)</sup>	43	18, 19, 20	2.7	-	11 (18G) 15 (19G)	-
Gorriz et al <sup>(40)</sup>	77	18	5.2	-	15.2	-

TJLB: transjugular liver biopsy, G: gauge, PT: portal tracts,

\* = in 14 cirrhotics,

<sup>†</sup> = length per core, <sup>‡</sup> = 1.2 mm needle diameter.

G: gauge [translation of gauge (G) to external diameter of needle in millimetre (mm): 14G=2.1mm, 15G=1.83mm, 16G=1.65mm, 17G=1.47mm, 18G=1.24mm, 19G=1.06mm]

Our TJLB study using 3 passes per procedure in 326 biopsies (274 patients) is the largest evaluating quality. We focused our evaluation on the portal tract assessment using published criteria,[21] as Bravo et al[10] showed that portal tract number was the most reliable parameter and Colloredo et al,[14] stated "The critical factor influencing the negative effect of smaller

sizes is probably the significant drop in number of complete portal tracts in the smaller specimens”.

In our study, liver specimens were sufficient for diagnosis in 98.5%, similar to other TJLB studies using 18G needles,[18] [30] [37] or a 19G needle[20] as in ours. The median length was 22 mm, and most importantly, the median number of CP was 8. These results confirm the diagnostic efficacy of TJLB according to published guidelines[10] and show that TJLB with 3 passes, provides samples comparable to PLB from our centre and other series of PLB[23][27] [41]. In addition, as we showed in a recent review, the median length of PLB was 19.8 mm for Menghini, 14.5 mm for Trucut biopsy, and the median number of CP was 6.6 for Menghini biopsy and 5.8 for Trucut,[42] so that approximately 50% of PLB reported in series in the literature are suboptimal for diagnostic purposes. Importantly in our study, there was no major difference in the length, or number of fragments between cirrhotics and non-cirrhotics, whereas differences have been reported for percutaneous biopsies.[42] This may be due to our standardized procedure for handling TJLB. Fragmentation may occur following biopsy during transport to the histopathology laboratory, and usually has been reported on the fixed specimen and not at the time of biopsy.[42] In addition, the previously asserted inadequacy of TJLB for diagnosis of cirrhosis[29] was not confirmed. Our pathologists, using H&E, reticulin and Victoria blue stains, were always able to confirm the clinical diagnosis of cirrhosis, even from one sufficiently large fragment.

There were no differences in the number of CP nor in length nor in the proportions  $\geq 15$  mm or  $\geq 25$  mm long, in the biopsies performed for mainly diagnosis, mainly for staging/grading or from these groups when performed for both. Thus, TJLB with 3 passes almost always gives optimal biopsies for diagnosis (in contradistinction to data on PLB in the literature), but only results in adequate biopsies for staging/grading in 38% ( $\geq 25$  mm) or 25% ( $\geq 11$  CP).

Our study is also the first in which the number of CP and PPT has been evaluated in a TJLB series. The median CP:PPT ratio was 1.6:1, but only a modest correlation was found between total length and total number of CP ( $r=0.49$ ). This finding is due to 2 possible reasons. Firstly the small diameter of liver samples and secondly fragmentation. The 19G needle has an external diameter of 1 mm and internal diameter (which in fact determines the maximum width of the liver core) of approximately 0.9 mm. However, the width in several fragments was less than 0.5 mm or was variable, even in the same fragment. Crawford et al[21] and Menghini,[43] also found variable and smaller biopsy widths ( $0.9\pm 0.3$ mm and average 0.75mm diameter, respectively) than the internal needle diameter, when using 14G or a 1.5 mm diameter Menghini needle. In our study, using Trucut needle, this phenomenon may be exacerbated due to the fact that the slot in the Trucut needle is not cylindrical i.e. the height of the space is less than its width. The range of widths is due to the microtome cutting planes through the biopsy core not always going through its maximum diameter, so that internal needle diameter is not equivalent to biopsy width. In addition there is tissue shrinkage with fixation embedding and some twisting of the tissue core. As a result, in our study, several lengthy fragments contained very few or even no CP, but nevertheless  $\geq 11$  CP were obtained with core widths  $\leq 1$  mm, in contradistinction to Colloredo et al.[14] Using an 18G needle could improve

this, but requires further evaluation because it is less flexible and has been reported to increase the fragmentation rate.[20] [40]

From our assessment of the number of CP and PPT in each fragment, using 3 passes, it can be estimated that 50% of 3 non-fragmented cores of 23 mm total length would contain 11 CP. However, in clinical practice, fragmentation can not be eliminated completely, but improvements might be made by more careful handling of TJLB samples. In our cohort the median total length (in order to contain 11 CP) was 28 mm taking into account fragmentation.

In summary, obtaining at least 3 cores at each TJLB was safe, and resulted in a median length of 22 mm independent of the presence of cirrhosis. The median number of CP was 8 and of PPT was 5. There was an average of 5 fragments in each TJLB. Reduction of fragmentation and/or modification of the length of the notch in the Tru cut device would increase the number of CP. The characteristics of our TJLB with 3 passes, are better than the average PLB reported in the literature.[23][27] [41][42]

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article (if accepted) to be published in Gut editions and any other BMJ PGL products to exploit all subsidiary rights, as set out in our licence (<http://gut.bmjournals.com/misc/ifora/licenceform.shtml>)."

We declare no competing interests

## REFERENCES

1. Campbell MS, Reddy KR. Review article: the evolving role of liver biopsy. *Aliment Pharmacol Ther* 2004;**20**:249-259.
2. Lebrech D. Various approaches to obtaining liver tissue--choosing the biopsy technique. *J Hepatol* 1996;**25 Suppl 1**:20-24.
3. Silecchia G, Raparelli L, Perrotta N, et al. Accuracy of laparoscopy in the diagnosis and staging of lymphoproliferative diseases. *World J Surg* 2003;**27**:653-658.
4. DeWitt J, LeBlanc J, McHenry L, et al. Endoscopic ultrasound-guided fine needle aspiration cytology of solid liver lesions: a large single-center experience. *Am J Gastroenterol* 2003;**98**:1976-1981.
5. Babb RR, Jackman RJ. Needle biopsy of the liver. A critique of four currently available methods. *West J Med* 1989;**150**:39-42.
6. Grant A, Neuberger J. Guidelines on the use of liver biopsy in clinical practice. British Society of Gastroenterology. *Gut* October 2004;on line.
7. Burroughs AK, Dagher L. Liver biopsy. In: Classen M, Tytgat G, and Lightdale C, eds. *Gastrointestinal Endoscopy*. New York, Thieme New York 2002:252-259.
8. Mayoral W, Lewis JH. Percutaneous liver biopsy: what is the current approach? Results of a questionnaire survey. *Dig Dis Sci* 2001;**46**:118-127.
9. Tobkes AI, Nord HJ. Liver biopsy: review of methodology and complications. *Dig Dis* 1995;**13**:267-274.
10. Bravo AA, Sheth SG, Chopra S. Liver biopsy. *N Engl J Med* 2001;**344**:495-500.
11. McAfee JH, Keeffe EB, Lee RG, et al. Transjugular liver biopsy. *Hepatology* 1992;**15**:726-732.
12. Piccinino F, Sagnelli E, Pasquale G, et al. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. *J Hepatol* 1986;**2**:165-173.
13. Schlichting P, Holund B, Poulsen H. Liver biopsy in chronic aggressive hepatitis. Diagnostic reproducibility in relation to size of specimen. *Scand J Gastroenterol* 1983;**18**:27-32.
14. Colloredo G, Guido M, Sonzogni A, et al. Impact of liver biopsy size on histological evaluation of chronic viral hepatitis: the smaller the sample, the milder the disease. *J Hepatol* 2003;**39**:239-244.

15. Bedossa P, Dargere D, Paradis V. Sampling variability of liver fibrosis in chronic hepatitis C. *Hepatology* 2003;**38**:1449-1457.
16. Kardache M, Soyer P, Boudiaf M, et al. Transjugular liver biopsy with an automated device. *Radiology* 1997;**204**:369-372.
17. De Hoyos A, Loredó ML, Martínez-Ríos MA, et al. Transjugular liver biopsy in 52 patients with an automated Trucut-type needle. *Dig Dis Sci* 1999;**44**:177-180.
18. Bruzzi JF, O'Connell MJ, Thakore H, et al. Transjugular liver biopsy: assessment of safety and efficacy of the Quick-Core biopsy needle. *Abdom Imaging* 2002;**27**:711-715.
19. Bull HJ, Gilmore IT, Bradley RD, et al. Experience with transjugular liver biopsy. *Gut* 1983;**24**:1057-1060.
20. Choh J, Dolmatch B, Safadi R, et al. Transjugular core liver biopsy with a 19-gauge spring-loaded cutting needle. *Cardiovasc Intervent Radiol* 1998;**21**:88-90.
21. Crawford AR, Lin XZ, Crawford JM. The normal adult human liver biopsy: a quantitative reference standard. *Hepatology* 1998;**28**:323-331.
22. MacSween R, Desmet V, Roskams T. Developmental anatomy and normal structure. In: MacSween RN, Burt A, Portmann B, Ishak K, Scheuer PJ, and Anthony P, eds. *Pathology of the liver*. London, Churchill Livingstone 2002:1-66.
23. Rocken C, Meier H, Klauck S, et al. Large-needle biopsy versus thin-needle biopsy in diagnostic pathology of liver diseases. *Liver* 2001;**21**:391-397.
24. Petz D, Klauck S, Rohl FW, et al. Feasibility of histological grading and staging of chronic viral hepatitis using specimens obtained by thin-needle biopsy. *Virchows Arch* 2003;**442**:238-244.
25. Siddique I, El Naga HA, Mada JP, et al. Sampling variability on percutaneous liver biopsy in patients with chronic hepatitis C virus infection. *Scand J Gastroenterol* 2003;**38**:427-432.
26. Demetris AJ, Ruppert K. Pathologist's perspective on liver needle biopsy size? *J Hepatol* 2003;**39**:275-277.
27. Colombo M, Del Ninno E, de Franchis R, et al. Ultrasound-assisted percutaneous liver biopsy: superiority of the Tru-Cut over the Menghini needle for diagnosis of cirrhosis. *Gastroenterology* 1988;**95**:487-489.
28. Lebec D, Goldfarb G, Degott C, et al. Transvenous liver biopsy: an experience based on 1000 hepatic tissue samplings with this procedure. *Gastroenterology* 1982;**83**:338-340.

29. Gamble P, Colapinto RF, Stronell RD, et al. Transjugular liver biopsy: a review of 461 biopsies. *Radiology* 1985;**157**:589-593.
30. Smith TP, Presson TL, Heneghan MA, et al. Transjugular biopsy of the liver in pediatric and adult patients using an 18-gauge automated core biopsy needle: a retrospective review of 410 consecutive procedures. *AJR Am J Roentgenol* 2003;**180**:167-172.
31. McGill DB, Rakela J, Zinsmeister AR, et al. A 21-year experience with major hemorrhage after percutaneous liver biopsy. *Gastroenterology* 1990;**99**:1396-1400.
32. Gilmore IT, Bradley RD, Thompson RP. Improved method of transvenous liver biopsy. *Br Med J* 1978;**2**:249.
33. Papatheodoridis GV, Patch D, Watkinson A, et al. Transjugular liver biopsy in the 1990s: a 2-year audit. *Aliment Pharmacol Ther* 1999;**13**:603-608.
34. Choo SW, Do YS, Park KB, et al. Transjugular liver biopsy: modified Ross transseptal needle versus quick-core biopsy needle. *Abdom Imaging* 2000;**25**:483-485.
35. DiMichele DM, Mirani G, Wilfredo CP, et al. Transjugular liver biopsy is safe and diagnostic for patients with congenital bleeding disorders and hepatitis C infection. *Haemophilia* 2003;**9**:613-618.
36. Chau TN, Tong SW, Li TM, et al. Transjugular liver biopsy with an automated trucut-type needle: comparative study with percutaneous liver biopsy. *Eur J Gastroenterol Hepatol* 2002;**14**:19-24.
37. Elsharkawy A, Austin A, Ryder S. Clinical impact of transjugular liver biopsies in a non-transplant center [abstract]. *Hepatology* 2002:P728.
38. Regan J, Mihalov M, Limjoko A, et al. Transjugular liver biopsy: evaluation and comparison with percutaneous biopsy [abstract]. *Hepatology* 1997;**26**(suppl 1):P281.
39. Little AF, Zajko AB, Orons PD. Transjugular liver biopsy: a prospective study in 43 patients with the Quick-Core biopsy needle. *J Vasc Interv Radiol* 1996;**7**:127-131.
40. Gorriz E, Reyes R, Lobrano MB, et al. Transjugular liver biopsy: a review of 77 biopsies using a spring-propelled cutting needle (biopsy gun). *Cardiovasc Intervent Radiol* 1996;**19**:442-445.
41. Farrell RJ, Smiddy PF, Pilkington RM, et al. Guided versus blind liver biopsy for chronic hepatitis C: clinical benefits and costs. *J Hepatol* 1999;**30**:580-587.
42. Cholongitas E, Senzolo M, Standish R, et al. A systematic review of

the quality of liver biopsy specimens. *Am J Clinical Pathology* 2006 (in press).

43. Menghini R. One-second needle biopsy of the liver. *Gastroenterology* 1958;**35**:190-199.

## FIGURE LEGENDS

**Figure 1.** Non parametric correlation between total length and complete portal tracts in the 194 transjugular liver biopsies in which portal tracts could be counted (Spearman  $r=0.49$ ,  $p<0.001$ ).

**Figure 2.** Fragment length and number in 1045 fragments in 194 evaluable biopsies and relationship between number of complete portal tracts and fragment length and number.



