

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4436

**Title:** Radiofrequency ablation of hepatocellular carcinoma sized  $>3$  and  $\leq 5$  cm: is ablative margin of more than 1 cm justified?

**Reviewer code:** 00054683

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-06-29 21:12

**Date reviewed:** 2013-07-03 21:51

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

1) The median diameter of the HCC nodules was  $4.2 \pm 0.4$  cm (range: 3.1-5.0). Median value should be not reported with standard deviation. Please remove SD or alternatively, report mean and SD, and median and range in parenthesis. 2) If a randomization was not performed in this study what was the basis of the choice for 0.5 or 1.0cm AM target? Presence of vessels? Radiologist/ hepatologist in charge? Please describe better your approach. 3) the distinction if group A and B is confusive. There are only two groups and it is not necessary to re-nominate them. Please use 0.5-1.0cm and  $>1$ cm as group names. 4) In the title of the paragraph "Evaluation of AM" the abbreviation AM should be reported for its entire meaning. 5) Continuous data were expressed as mean  $\pm$  SD and were compared using Mann-Whitney U test. However, Mann-Whitney U test is a non-parametric analysis, and this is in contrast with the choice to report data as mean and SD. If authors checked their data for normality they should use student t-test, alternatively, please report continuous data in median and range. Of note that AFP, reported as mean and SD, evidently has a non-normal distribution. This feature supports the need to completely change table 1 reporting medians and ranges. 6) Please explain better if TACE was performed (in all patients) with the aim of radiological assessment of AM or for oncological purposes. 7) Results: (44.7%) of 123 patients in the group B ( $P = 0.000$ ). P-value is not correct; please change it in  $P < 0.001$ . The same must be done with the other  $P = 0.000$  in the manuscript. 8) In table 1, please report percentages for categorical variables. 9) Please clarify why you use chi-square with Yates correction or Fisher for 2x2 tables. Fisher's exact test is a more accurate test, which directly calculates the probability of the distribution of the sample appearing in the table by chance. I suggest using Fisher in all cases, for large sample sizes Fisher and



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Chi-square will produce very similar results. 10) In table 3, please add in the footnote the analysis that provided p-values (Cox regression as reported in methods) 11) Kaplan - Meier curves should be reported together with a footnote reporting patients at risk for specific time points. 12) In the discussion section, the statement "Extensive clinical studies support RF ablation as an efficient, less invasive, and well preferred treatment for early HCC patients with tumor diameters  $\leq 5.0$  cm" is not supported by any international guideline; conversely RFA can be a preferred treatment for very early HCC [EASL and AASLD guidelines]. This statement needs to be changed.

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**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4436

**Title:** Radiofrequency ablation of hepatocellular carcinoma sized  $>3$  and  $\leq 5$  cm: is ablative margin of more than 1 cm justified?

**Reviewer code:** 02506941

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-06-29 21:12

**Date reviewed:** 2013-08-08 14:28

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input checked="" type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

Please explain the abbreviation TAE; I suppose is Trans-Arterial Embolization, however, if was used in the text, it should be explained (page 11 of the manuscript, bottom of page)

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**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4436

**Title:** Radiofrequency ablation of hepatocellular carcinoma sized  $>3$  and  $\leq 5$  cm: is ablative margin of more than 1 cm justified?

**Reviewer code:** 00200689

**Science editor:** Song, Xiu-Xia

**Date sent for review:** 2013-06-29 21:12

**Date reviewed:** 2013-08-19 22:00

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

"The diagnosis of HCC was established on the basis of compatible radiological features with HCC in contrast-enhanced multiphase helical CT scan and dynamic contrast-enhanced MRI (n = 155) and histological confirmation (n = 126). " Please elaborate it. "The aim of this study was explained to all of the approved patients in advance, a safe AM of  $> 1.0$  cm was tried in all the patients although an AM of  $\geq 0.5$  cm was routinely considered enough. On the basis of the AM, we categorized patients into group A (AM of 0.5-1.0 cm) and group B (AM  $> 1.0$  cm). " How do you define the AM  $> 1.0$  cm or not? Please make it clear. "TACE was performed 2-3 weeks before RF ablation ". In my understanding, TACE was performed in all the cases. So the title should be revised to include TACE. "RF generator (RITA 1500, RITA Medical Systems Inc, Manchester, GA, USA) or (Covidien Healthcare, Ireland) was used according to the manufacturer's protocol, respectively. " Please describe the procedures in detail. "In the evaluation, the AM was defined as the narrowest width of the area of low density outside the iodine stain " This may have bias if the iodine stain in the tumor is not uniform or the tumor is hypovascular. Please discuss it. Results "During the follow-up, LTP was found in 112 (70.9%) of 158 patients in the group A and in 55 (44.7%) of 123 patients in the group B (P = 0.000) (Table 2). The rates of LTP only and total LTP in the group A were significantly higher than these in the group B (46.8% and 70.9% vs. 31.7% and 44.7%, P = 0.010, 0.000 respectively). The 1-, 2-, 3-, 4-, and 5-year LTP-free survival rate was 91.3%, 78.4%, 49.5%, 27.8%, and 12.8% in the group A and 97.5%, 86.3%, 73.6%, 49.5% and 26.4% in the group B, respectively (Fig. 3), with statistical difference between the two groups (P = 0.001). " The LTP is substantially high, which lead to uncertainty about the author's skill. On the other hand, the LTP-free survival rate is very high. It seems incompatible.

Please explain it. "liver unrelated diseases in 4 (5.1%), and undetermined in 6 (7.7%) " Please elaborate it. The following articles might be useful for the authors to make revision: Zheng SG, Xu HX, Lu MD, Xie XY, Xu ZF, Liu GJ, Liu LN. The role of contrast-enhanced ultrasound in follow-up assessment after percutaneous ablation therapy for hepatocellular carcinoma. *World J Gastroenterol*, 2013 Feb 14;19(6):855-65. Liu LN, Xu HX, Zhang YF, Xu JM. Hepatocellular carcinoma after ablation: the imaging follow-up scheme. *World J Gastroenterol*, 2013 Feb 14;19(6):797-801. Xu HX, Lu MD, Liu LN, Guo LH. Magnetic navigation in ultrasound-guided interventional radiology procedures. *Clin Radiol*. 2012;67(5):447-54. Xu HX, Wang Y, Lu MD, Liu LN. Percutaneous ultrasound-guided thermal ablation for intrahepatic cholangiocarcinoma. *Br J Radiol*. 2012 Aug;85(1016):1078-84. Xu HX, Lu MD, Xie XH, Xie XY, Kuang M, Xu ZF, Liu GJ, Wang Z, Chen LD, Lin MX. Treatment response evaluation with three-dimensional contrast-enhanced ultrasound for liver cancer after local therapies. *Eur J Radiol*. 2010 Oct;76(1):81-8.