



Liver Resection and Role of Extended Cytology and Histology

Response to: Viganò L, Costa G, Cimino MM, Procopio F, Donadon M, Del Fabbro D, Belghiti J, Kokudo N, Makuuchi M, Vauthey JN, Torzilli G. R1 Resection for Colorectal Liver Metastases: a Survey Questioning Surgeons about Its Incidence, Clinical Impact, and Management. *J Gastrointest Surg.* 2018 Oct; 22(10):1752–1763

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Dear Editor

We read the article by Viganò L et al.¹ with interest. The study clearly reflects the shifting paradigm to accept positive margin status (R1) as a part of the multidisciplinary management of colorectal liver metastases (CRLM) and that it is not just a technical issue. Liver resection is the most effective treatment for patients with CRLM confined to the liver, with reported actuarial survival rates approaching 58% at 5 years.² Parenchymal preservation surgery is one of the major operative modalities of resecting the metastatic liver disease. The positive margin (R1) status is proved to be an independent prognostic factor associated with a negative effect on patient survival (mean 5-year survival—17% versus 67% in patients with positive and negative margins respectively).^{2,3} The three-dimensional growth of the tumour could result in proximity of the tumour to the blood vessels and bile ducts that and is one of the primary reasons for a closer margin to the tumour; misjudgement of the margin by the surgeon is sometimes a possibility.

It is important to note that unlike tumours of the skin or soft tissue where a knife or a diathermy gives a sharp cut occupying a width of 1–2 mm, parenchymal transection of liver is performed with an energy device such as CUSA (Cavitron ultrasonic surgical aspirator) or Lotus/Harmonic scalpel that are space occupying by up to 4–5 mm width. This might mean that although the tumour is close on the specimen side

(reported as R1 on the histopathology specimen), there may not be any tumour cells left on the patient resulting in an R0 resection. Perhaps, this discrepancy might explain the reason why only 40–60% of the margin-positive patients actually have local recurrence.

For patients with a close tumour margin (on the specimen side), if there are tumour cells on the patient side after the liver resection, we should ideally be offering further treatment such as chemotherapy or local ablation procedures at the time of surgery. However, to date, there is no clear consensus on the management of R1 liver resection in CRLM. With only half of the patients developing long-term recurrence at margin-positive sites, it is probably not possible to obtain high-quality evidence to support adjuvant chemotherapy, local treatment or wait and watch policy in such scenarios.

Does this mean we should consider moving towards ‘extended cytological or histological’ assessment of the patient side of non-anatomical liver resections rather than being guided by the histological assessment of the resected specimen? Should the near-future research focus on assessing the role of forgotten techniques such as imprint cytology or further intra-operative molecular evaluation to assess the patient side of liver resection?

We performed 14 non-anatomical resections for a patient with 19 bilobar deposits of CRLMs. At the time of resection, where we assessed the margin to be close, we performed further CUSA of the base and retrieved the specimen in a separate pot for histological assessment. Figure 1 shows the histological assessment of the margin-positive specimen and Fig. 2 shows that the CUSA specimen of the base was negative for tumour cells. The CUSA device only causes fragmentation of tissues and should provide an adequate histological specimen.

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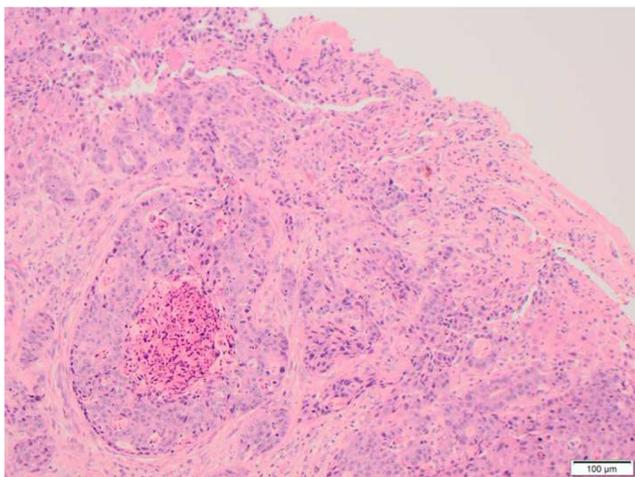


Fig. 1 Tumour cells within 1 mm of the resected specimen indicating margin positivity

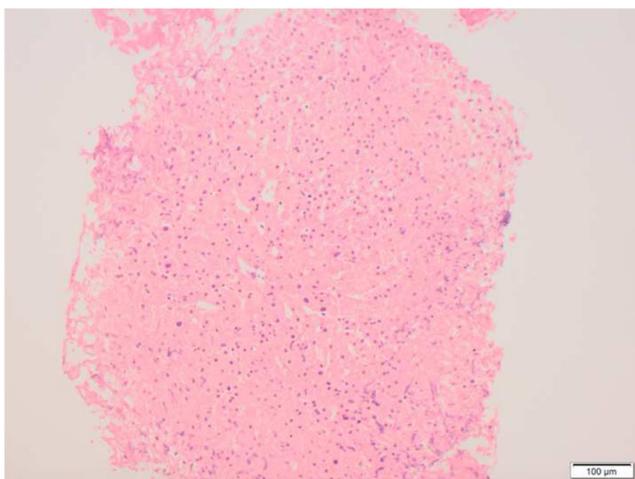


Fig. 2 Absence of tumour cells in the CUSA specimen from the patient side of non-anatomical liver resection

We also explored if imprint cytology (IC) was useful in the liver resection specimen. Figure 3 demonstrates the cancer cells visualised on the cytological evaluation of the margin-positive specimen. For the imprint of the specimen, the cut surface of the specimen was wiped off the excessive blood if present followed by imprints taken on the slides. All relevant representative surfaces were used for imprint cytology. These slides were dried and immediately immersed in to 95% ethyl alcohol and subsequently sent for staining and evaluation. Three out of the four imprints taken on the specimen side correlated with the final histological evaluation. Whether similar results can be obtained on the patient side (base of resection) and the longer-term influence of this methodology needs

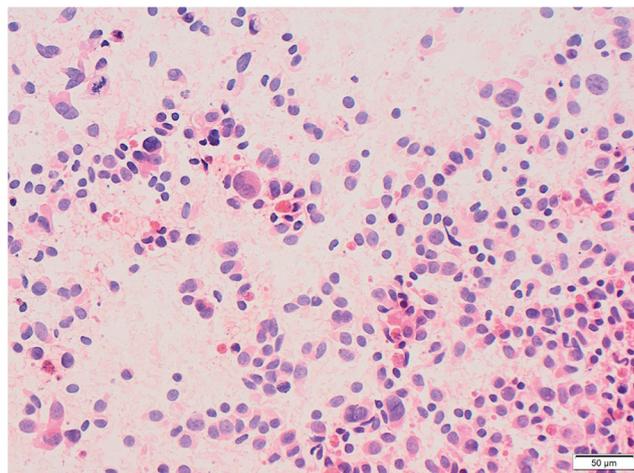


Fig. 3 Tumour cells on imprint cytology of the resected specimen

to be further evaluated. Prospective multi-centre collaborative clinical research studies might help answering these questions.

We believe that there is a role for such ‘extended histological or cytological’ assessment of the patient side of non-anatomical liver resections rather than the specimen side in the future management of these patients. If these techniques prove feasible and reliable in predicting long-term outcomes, we might need to consider redefining margin positivity to be evaluated on the patient side of the resection rather than the specimen side.

References

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