

**Comment on: “Indications and results of diagnostic biopsy in pediatric renal tumors: A retrospective analysis of 317 patients with critical review of SIOP guidelines”**

Thomas J Jackson<sup>1\*</sup>, Gordan M Vujanic<sup>2</sup>, Kathy Pritchard-Jones<sup>1</sup>

<sup>1</sup> University College London Great Ormond Street Institute of Child Health, London, UK

<sup>2</sup> Sidra Medicine, Doha, Qatar

\*Corresponding Author: Thomas J Jackson, Academic Clinical Fellow, University College London Great Ormond Street Institute of Child Health, 30 Guilford Street, London, UK WC1N 1EH.

Email: thomas.jackson4@nhs.net

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We read with interest the article of de la Monneraye et al. on the experience of the Institut Curie of renal tumour biopsy in children treated according to SIOP protocols over a 22 year period<sup>1</sup>.

By presenting the relative proportion of children with non-Wilms tumours who had clinical, radiological and biochemical features that are considered “atypical” of Wilms tumours (WT) they support a change to an evidence-based approach to biopsy in the SIOP community. However, some of their recommendations are not adequately supported by a single institutional series and we would like to add some reflections from our work based on national and population-level data.

First, they rightly identify that if age alone is the criterion to biopsy to identify non-WT then 6 years is an inappropriately low cut-off. They are also right that biopsy could be considered for infants between 3-6 months, as in this age group benign tumours are a minority of cases in their series and others<sup>2-4</sup>. However, raising the upper age criteria to 9 years is taken from a Figure where they have grouped 9-12 years together – why not choose 10, 11 or 12 years? Comparing tumour distribution amongst the incident population rather than a single institution’s referral practice is more accurate. Based on English National Cancer Registry data from 2006-2015 the age of inflection point when WT changes from 83% to 38% of paediatric renal tumours is from 10 to 11 years<sup>2</sup>. On this basis we suggest an age of 10 years and older as a cut-off<sup>2</sup>.

Second, they state upfront surgery should be considered for children with small volume tumours as “chemoreduction” is unnecessary. However, tumour size is not necessarily related

to risk of tumour rupture. Children who were not randomised in the UKW3 trial and had elective immediate nephrectomy had smaller median tumour size and yet had significantly higher rupture rates than those who received pre-operative therapy<sup>5</sup>. Furthermore, pre-operative chemotherapy allows for stratification based on chemo-responsiveness irrespective of reducing rupture risk.

Third, their claim in the discussion that a large tumour volume discriminates between WT and non-WT after adjustment for age is not supported by appropriate statistical analysis. The distribution of tumour volumes in Figure 2 shows both CCSK and WT may be large (>500ml) at presentation. Clearly a larger study, better powered to identify any potential volume threshold, is needed.

Fourth, they overstate the utility of FNA to replace or adjunct cutting needle biopsy. Biopsy type does not determine the possible genetic analyses; necrotic samples are rare if image guidance is used; coagulopathy is a contraindication for any biopsy using a coaxial technique and their cited study of adult practice is underpowered and not obviously applicable to a paediatric context.

Finally, two errata. 1) Vujanic *et al.*,<sup>6</sup> reports the incidence of specific complications from 0.5-20% not a total complication rate of 1.2% as cited, 2) Irtan *et al.*, (reference 61) should be attributed for the analysis of relapse risk after biopsy in the UKW3 trial not reference 62.

1. de la Monneraye, Y. *et al.* Indications and results of diagnostic biopsy in pediatric renal tumors : A retrospective analysis of 317 patients with critical review of SIOP guidelines. *Paediatr. Blood Cancer* 1–11 (2019). doi:10.1002/pbc.27641

2. Jackson, T. J. *et al.* The diagnostic accuracy and clinical utility of pediatric renal tumor biopsy : Report of the UK experience in the SIOP UK WT 2001 trial. *Pediatr. Blood Cancer* (2019). doi:10.1002/pbc.27627
3. England, R. J. *et al.* Mesoblastic nephroma: A report of the United Kingdom children's cancer and leukaemia group (CCLG). *Pediatr. Blood Cancer* **56**, 744–748 (2011).
4. Gooskens, S. L. *et al.* Congenital mesoblastic nephroma 50 years after its recognition: A narrative review. *Pediatr. Blood Cancer* e26437 (2017). doi:10.1002/pbc.26437
5. Powis, M. *et al.* Surgical complications after immediate nephrectomy versus preoperative chemotherapy in non-metastatic Wilms' tumour: Findings from the 1991-2001 United Kingdom Children's Cancer Study Group UKW3 Trial. *J. Pediatr. Surg.* **48**, 2181–2186 (2013).
6. Vujanić, G. M., Kelsey, A., Mitchell, C., Shannon, R. S. & Gornall, P. The role of biopsy in the diagnosis of renal tumors of childhood: Results of the UKCCSG Wilms Tumor Study 3. *Med. Pediatr. Oncol.* **40**, 18–22 (2003).