Invited Editorial

# Uterine smooth muscle tumour of uncertain malignant potential (STUMP): Where are we now?

The spectrum of diagnoses of uterine mesenchymal tumours is continuously evolving. Until recently, these neoplasms were classified either as smooth muscle or as endometrial stromal neoplasms. The smooth muscle neoplasms were categorised as benign, malignant or smooth muscle tumours of uncertain malignant potential. With increasing sophistication of diagnosis and use of molecular techniques, there has been an expansion in the classification of tumour types and the distinction between these categories is becoming more refined.

The diagnosis of uterine smooth muscle tumours (USMTs) is, in most cases, straightforward. Most uterine smooth muscle tumours are benign. Leiomyosarcomas are diagnosed when a triad of histopathological features is seen - significant atypia, increased mitotic activity and coagulative/ tumour cell necrosis. However, USMTs can show a range of morphological and biological diversity and with the recognition that there are USMTs that defy a binary classification of diagnostic categories, the term smooth muscle tumour of uncertain malignant potential (STUMP) was introduced. This was done on the basis of a seminal paper [1] and has since been incorporated into the WHO classification. The 2014 WHO classification [2] defines STUMP as 'a smooth muscle tumour with features that preclude an unequivocal diagnosis of leiomyosarcoma, but does not fulfil the criteria for leiomyoma, or its variants, and raises concern that the neoplasm may behave in a malignant fashion'. There have been several studies of STUMP looking at predictors of behaviour within this subgroup. These include immunohistochemistry with PHH3, p53, PR, Ki67, Bcl-2 and alpha-SMA [3–5]. Whilst some of these markers have shown statistical significance in studies of case series when compared with leiomyomas or leiomyosarcomas, none has proved robust enough to incorporate into routine practice in the diagnosis of an individual case. It has been proposed that expansion of the histological criteria for STUMPs to include atypical mitoses, epithelioid differentiation, vascular involvement and infiltrative/irregular margins will allow better identification of the possibility of adverse outcomes [6]. There is promise of prediction of behaviour of STUMPs by genomic profiling. A recent study [7] has shown that genomic index with a cut-off = 10 is a predictor of recurrence ($P < .0001$) and with a cut-off = 35 is a marker for poor overall survival.

There are other unusual smooth muscle tumours such as intravascular leiomyomatosis, benign metastasizing leiomyoma, leiomyomas with bizarre nuclei and diffuse leiomyomatosis that have one or more features that can raise an alarm for unpredictable behaviour and may prompt a diagnosis of STUMP. With the increased application of molecular techniques, the non smooth muscle tumour categories have become more refined to include [8] high-grade endometrial stromal sarcomas with BCOR genetic abnormalities, fibrosarcoma-like uterine sarcomas with NTRK rearrangements and COL1A-PDGFRB fusions, inflammatory myofibroblastic tumours and solitary fibrous tumours. Some of these entities can resemble uterine smooth muscle tumours morphologically and immunohistochemically. It is plausible that the category of STUMPs has included some of these tumours.

So, the category of STUMP continues to be variably defined and as yet there is no definite marker of behaviour of an individual case. Pathologists need to be aware of the different entities that may be misdiagnosed as STUMP and clinicians need to be aware of the unpredictable behaviour in any single case.

## Contributors

Raji Ganesan is the sole author of this editorial.

## Conflict of Interest

The author has no conflict of interest regarding the publication of this editorial.

*Invited Editorial*

## Funding

No funding from an external source supported the publication of this editorial.

## Provenance and peer review

This editorial was commissioned and not externally peer reviewed.

## References

[1] S.W. Bell, R.L. Kempson, M.R. Hendrickson, Problematic uterine smooth muscle neoplasms. A clinicopathologic study of 213 cases, Am. J. Surg. Pathol. 18 (6) (1994 Jun) 535–558.

[2] E. Oliva, M.L. Carcangiu, S.G. Carinelli, et al., Tumours of the uterine corpus: Mesenchymal tumours: Smooth muscle tumour of uncertain malignant potential, in: R.J. Kurman, M.L. Carcangiu, C.S. Herrington, R.H. Young (Eds.), World Health Organization Classification of Tumors of Female Reproductive Organs, IARC Press, Lyon 2014, pp. 138–139.

[3] K.L. Chow, K.Y. Tse, C.L. Cheung, K.W. Wong, A.N. Cheung, R.W. Wong, A.N. Chan, N.W. Yuen, H.Y. Ngan, P.P. Ip, The mitosis-specific marker phosphohistone-H3 (PHH3) is an independent prognosticator in uterine smooth muscle tumours: an outcome-based study, Histopathology 70 (5) (2017 Apr) 746–755.

[4] D. Petrović, D. Babić, J.I. Forko, I. Martinac, Expression of Ki-67, P53 and progesterone receptors in uterine smooth muscle tumors. Diagnostic value, Coll Antropol. 34 (1) (2010 Mar) 93–97.

[5] S. Amada, H. Nakano, M. Tsuneyoshi, Leiomyosarcoma versus bizarre and cellular leiomyomas of the uterus: a comparative study based on the MIB-1 and proliferating cell nuclear antigen indices, p53 expression, DNA flow cytometry, and muscle specific actins, Int. J. Gynecol. Pathol. 14 (2) (1995 Apr) 134–142.

[6] M. Gupta, A.L. Laury, M.R. Nucci, B.J. Quade, Predictors of adverse outcome in uterine smooth muscle tumours of uncertain malignant potential (STUMP): a clinicopathological analysis of 22 cases with a proposal for the inclusion of additional histological parameters, Histopathology 73 (2) (2018 Aug) 284–298.

[7] S. Croce, A. Ducoulombier, A. Ribeiro, T. Lesluyes, J.C. Noel, F. Amant, L. Guillou, E. Stoeckle, M. Devouassoux-Shisheboran, N. Penel, A. Floquet, L. Arnould, F. Guyon, F. Mishellany, C. Chakiba, T. Cuppens, M. Zikan, A. Leroux, E. Frouin, I. Farre, C. Genestie, I. Valo, G. MacGrogan, F. Chibon, Genome profiling is an efficient tool to avoid the STUMP classification of uterine smooth muscle lesions: a comprehensive array-genomic hybridization analysis of 77 tumors, Mod. Pathol. 31 (5) (2018 May) 816–828.

[8] A. Momeni-Boroujeni, S. Chiang, Uterine mesenchymal tumours: recent advances, Histopathology 76 (1) (2020 Jan) 64–75.

Raji Ganesan
*Birmingham Women's Hospital, Mindelsohn Way, Birmingham, B15 2TG, United Kingdom*
*E-mail address:* r.ganesan@nhs.net

26 January 2020
Available online xxxx