

P. Ferreira de Oliveira, H. Almeida de Souza Cruz, S.R. Kleeb and J.G. Xavier
Patologia Ambiental e Experimental, Universidade Paulista, São Paulo, BR

INTRODUCTION

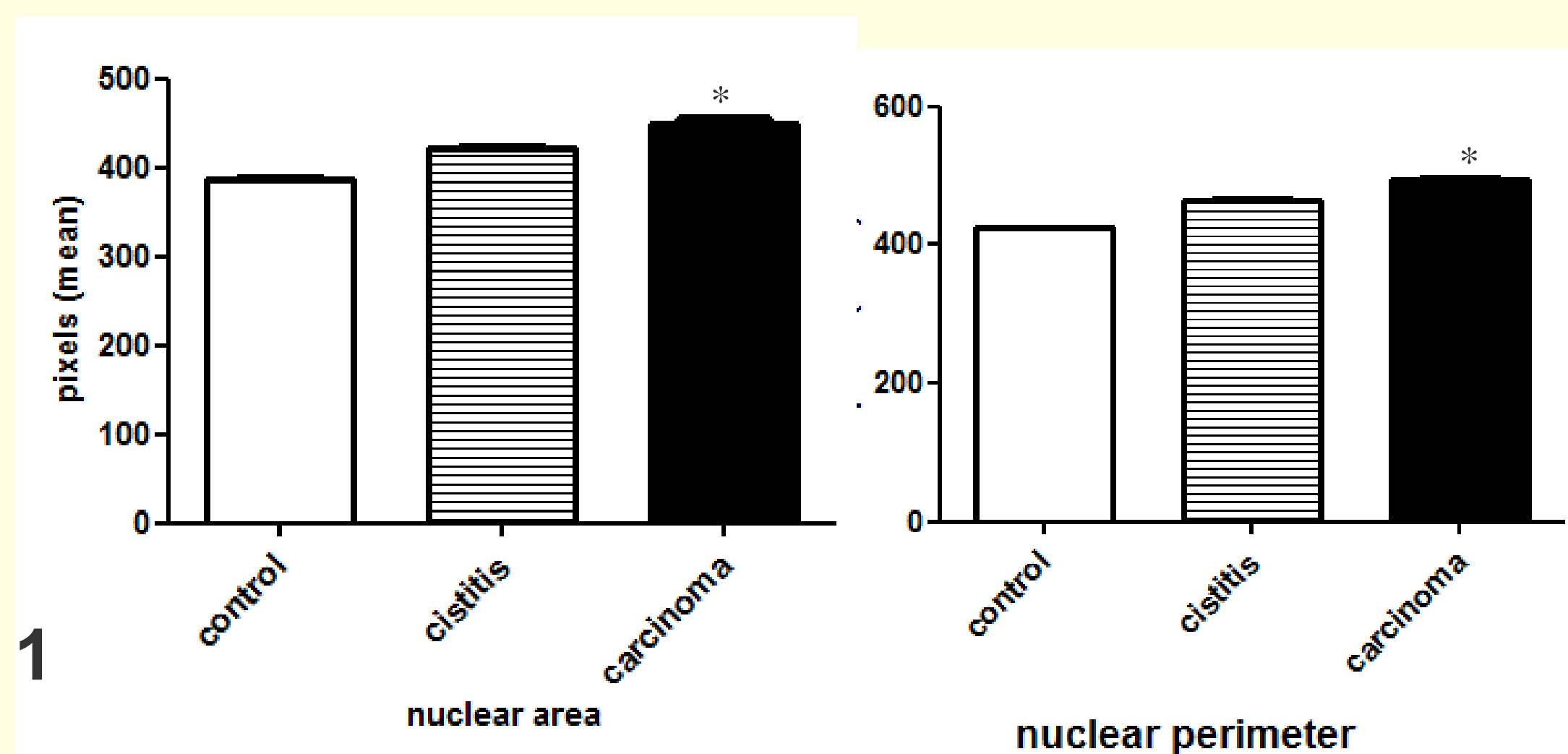
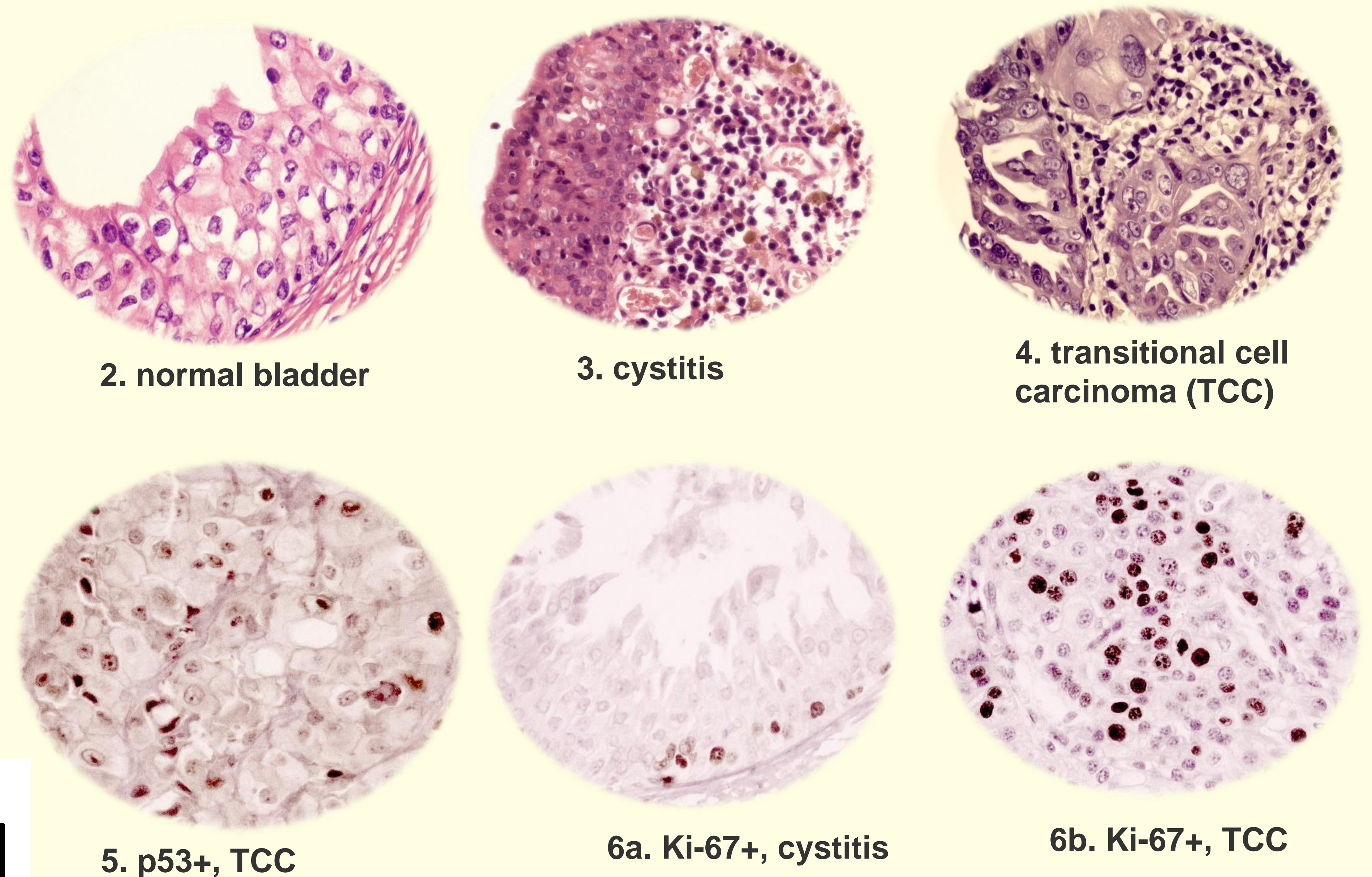
Canine transitional cell carcinomas (TCC) share many characteristics with human invasive urinary bladder TCC in terms of incidence, histopathology and biological behaviour. In humans, several markers have been proposed to monitor this disease, including oncogene products, proliferation markers and cell-cycle-related proteins. A frequent panel include CK20, p53 and Ki-67. The results are highly dependent on case selection, because the higher the grade and stage, the lower the CK20 detection rate, although conflicting findings have been reported. P53 and Ki-67 positivity is usually related with recurrence and survival rate. However, there are only few studies on this subject in canine urothelial lesions. This study aimed to assess the relationship of morphometric features and immunohistochemical markers with the histological diagnosis in canine bladder tissue.

MATERIALS AND METHODS

In this retrospective study, 25 samples of canine urinary bladder previously diagnosed as normal (n=5), cystitis (n=5), transitional cell carcinoma (TCC) (n=15), were subjected to a morphometric analysis, using a digital computerized analysis system (Metamorph®), evaluating urothelial nuclear area and perimeter. For each neoplasm, 200 nuclei, stained with HE were outlined by tracing their margins with the help of a computer mouse. In addition, immunohistochemistry was performed using the MACH 1 system (Biocare Medical) on 4 µm thick sections from formalin fixed, paraffin embedded blocks. MoAb to CK20 (Ks20, Biocare Medical), Ki-67 (MIB-1, Biocare Medical) and PoAb to p53 (FI393, Santa Cruz). Samples with known positive reactivity for each antibody were used as positive controls. As a negative control, a section was processed in which primary antibody was changed by PBS.

RESULTS

There was a statistically significant difference regarding the nuclear area and perimeter of urothelial cells between non-neoplastic (control-1, cystitis-2) and neoplastic samples (TCC-3) (Student's T test, $p < 0.0001$) (1). Immunorexpression of CK20 was infrequent in TCC (1/10). In contrast, p53 expression was observed only in neoplastic cells, in half of the TCCs (5). In TCCs, there was a qualitative and quantitative change in the proliferative profile evidenced by the more frequent and topographically wide immunorexpression of Ki-67 (6a-non neoplastic/6b-TCC). There was no relationship between histological parameters, such as muscle invasion and tumour embolization with immunohistological findings.



CONCLUSIONS

Nuclear morphometry and immunohistochemical parameters, as p53 and Ki-67 expression, can contribute to the characterization of canine transitional cell carcinomas.

REFERENCES

- Mallofré C, Castillo M, Morente V, Solé M. Immunohistochemical expression of CK20, p53, and Ki-67 as objective markers of urothelial dysplasia. *Mod Pathol*. 2003 Mar;16(3):187-91. doi: 10.1097/01.MP.0000056628.38714.5D.
- Meuten DJ. Tumors of the urinary system. In: Meuten DJ. *Tumors in domestic animals*, 5th ed., John Wiley & Sons, 2017.
- Sanguedolce F, Russo D, Calò B, Cindolo L, Carrieri G, Cormio L. Diagnostic and prognostic roles of CK20 in the pathology of urothelial lesions. A systematic review. *Pathol Res Pract*. 2019 Jun;215(6):152413. doi: 10.1016/j.prp.2019.04.005. Epub 2019 Apr 6. PMID: 30987832.
- Strefezzi Rde F, Xavier JG, Kleeb SR, Catão-Dias JL. Nuclear morphometry in cytopathology: a prognostic indicator for canine cutaneous mast cell tumors. *J Vet Diagn Invest*. 2009 Nov;21(6):821-5. doi: 10.1177/104063870902100608.