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# Classification and Epidemiology of Mammary Tumours in Pet Rabbits (*Oryctolagus cuniculus*)

**B. Baum*** **and M. Hewicker-Trautwein†**

** IDEXX Vet Med Labor GmbH, Ludwigsburg and † Department of Pathology, University of Veterinary Medicine Hannover, Germany*

## Summary

Mammary tumours are common in pet rabbits; however, published studies are predominantly derived from laboratory and meat rabbits. This study reports basic data on type and location of 119 separate tumours from 109 pet rabbits. The animals were aged 2–14 years (mean 5.5 years) and all 90 rabbits of known gender were female. Cranial and caudal mammary glands were affected equally. The majority of lesions ($n = 105$) were classified as carcinomas with 32 tubular, 16 papillary, 12 tubulopapillary, 11 solid, nine adenosquamous, nine comedo type, five complex, four ductal, three cribriform, three anaplastic and one spindle -cell carcinoma. Twelve percent of the lesions were benign, with eight intraductal papillary adenomas, three simple tubular adenomas and one complex adenoma. One non-neoplastic lesion was found in the form of cystic duct ectasia.



*Keywords:* classification; mammary gland; rabbits; tumour

## Introduction

The numbers of biopsy submissions from rabbits to diagnostic pathology laboratories are increasing. The majority of these samples come from individual pet rabbits. In textbooks, the frequency of mammary tumours in rabbits is variably described as 'rare' (Misdorp, 2002) or 'reported with fair frequency' (Weisbroth, 1994), referring in both cases to laboratory rabbits. In contrast, among the submissions to the German Division of IDEXX Laboratories, mammary tumours are common, comprising about 20% of all submissions from pet rabbits (unpublished data). However, to our knowledge, epidemiological and histopathological data on the types of mammary tumours in pet rabbits are not available. The aim of the present study was to summarize data from 109 rabbits with mammary tumours. Biopsy samples from these animals were submitted for diagnosis between 2010 and 2012.

## Materials and Methods

Samples of formalin-fixed rabbit mammary masses were processed routinely and embedded in paraffin wax. Sections were stained with haematoxylin and eosin (HE). Every submission of a mammary mass from a rabbit submitted over this time period was included in the investigation and no preselection of cases was made. Where a rabbit had multiple tumours, these were only counted separately if they were of a different type. A total of 119 tumours were examined from 109 rabbits, out of a total of 531 submissions of rabbit biopsy samples over the study period.

Clinical data were taken from the submission form. Gender, age, size of the tumour and identity of affected mammary glands were compared and evaluated statistically for the arithmetic mean value and standard deviation, where applicable. Age of onset and size of tumour for carcinomas and benign lesions were compared with the Student's t-test. Animals with incomplete data were omitted from the analysis of those criteria.

Tumour morphology was assessed microscopically for histological pattern, cytological appearance,

Correspondence to: B. Baum (e-mail: berit-baum@idexx.com).

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tumour growth pattern and inflammation. A scoring system was developed for semiquantitative morphological analysis (Table 1). Diagnosis was made according to the World Health Organisation histological classification for mammary tumours in cats and dogs (Misdorp *et al*., 1999) applying the current modification for canine mammary tumours (Goldschmidt *et al*., 2011).

## Results

*Clinical Features*

The age of 89 rabbits with mammary tumours ranged from 2 to 14 years (mean of 5.5 years). The mean age for animals with carcinomas was significantly higher than that for those with adenomas ($P < 0.05$; Table 2). Cranial and caudal mammary glands were affected almost identically for carcinomas (Table 3), but the low number of benign lesions did not allow statistical evaluation. The left and right mammary chains did not differ substantially in the frequency of lesions. The size of the entire lesion at the time of submission ranged from 4 to 100 mm. Benign lesions were significantly smaller than carcinomas ($P < 0.01$).

*Histological Appearance*

Mammary epithelial cells were often heavily vacuolated, most likely caused by the presence of fat globules (Fig. 1). The degree of vacuolation varied considerably between individuals, even when they had comparable tumours. Complex and ductal carcinomas appeared to be more often lipid rich, but in these categories too few animals were examined for statistical evaluation of this impression.

The dominant tumour type was the simple neoplasm (Fig. 2). Tubular (Fig. 3), cystic–papillary (Fig. 4) and combined forms comprised about half of the carcinomas and the majority of adenomas. Among carcinomas, four cases of ductal origin were diagnosed, based on the presence of duct-like bilayered formations in combination with squamous differentiation. Advancing de-differentiation was evident in 12 predominantly cribriform or anaplastic tumours and in the single spindle -cell carcinoma.

**Table 1**
**Microscopical criteria evaluated in rabbit mammary tumours and key to scoring system**

| | | |
|---|---|---|
| **Histological appearance** | Growth type | Tubular |
| | | Papillary |
| | | Solid |
| | | Cribriform |
| | Tubule formation | Percentage of tumour area involved |
| **Cytological appearance** | Cell shape | Columnar (1) |
| | | Cuboidal (2) |
| | | Polygonal to rounded (3) |
| | Pleomorphism | Monomorphic to mildly pleomorphic (1) |
| | | Moderately pleomorphic (2) |
| | | Markedly pleomorphic (3) |
| | Mitotic rate | Mitoses per 10 HPFs (×400) in active areas |
| | Cells with fat vacuoles | Percentage of tumour cells affected |
| | Areas with squamous differentiation | Percentage of tumour area affected |
| **Growth pattern** | Pattern (% of tumour area with this pattern) | Intraluminal |
| | | Expansile |
| | | Infiltrative |
| | Stroma | Scant (1) |
| | | Moderate (2) |
| | | Scirrhous (3) |
| | Invasion of the dermis | Yes/no |
| | Invasion of the musculature | Yes/no |
| **Inflammation** | Ulceration | Yes/no |
| | Number of heterophilic granulocytes | Few disseminated cells (1) |
| | | Multiple nests of cells (2) |
| | | Aggregates of cells (3) |
| | Number of lymphocytes | Few disseminated cells (1) |
| | | Multiple nests of cells (2) |
| | | Aggregates of cells or follicles (3) |

1, 2 and 3 define the scoring system used to assess the morphological criteria semiquantitatively.