

NTP Nonneoplastic Lesion Atlas

Mammary Gland – Fibrosis

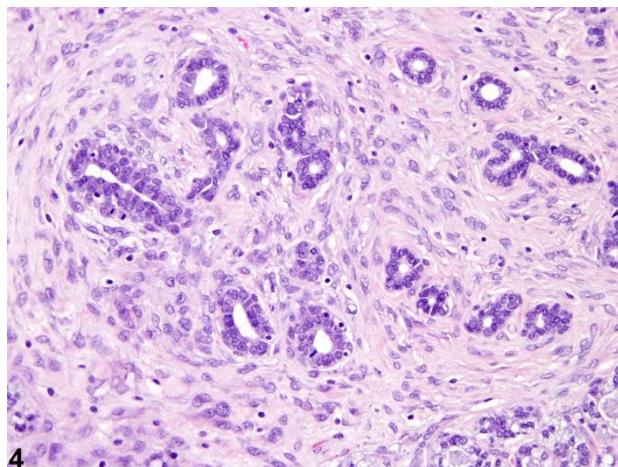
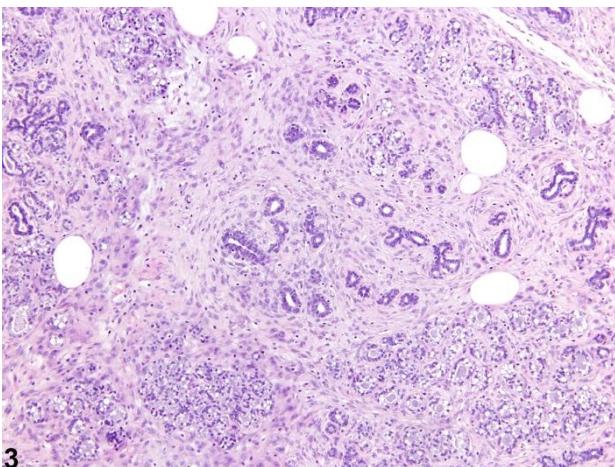
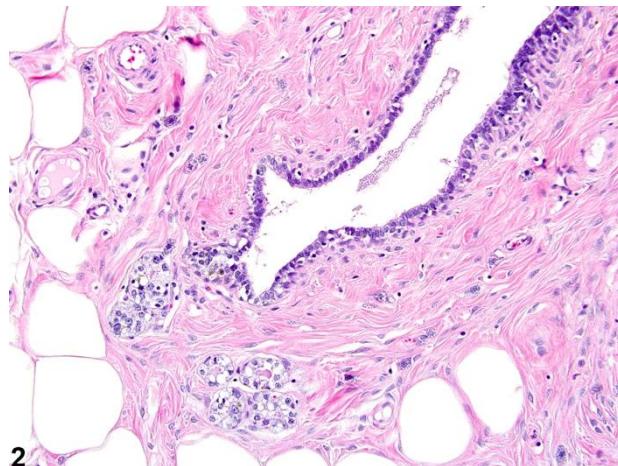
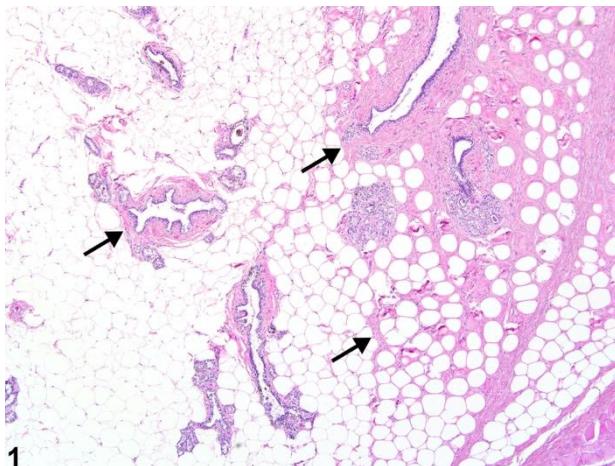


Figure Legend: **Figure 1** Mammary gland - Fibrosis in a male F344/N rat from a chronic study.

Mammary gland fibrosis is characterized by increased amounts of mature fibrous connective tissue both surrounding mammary gland ducts and extending into the adjacent mammary adipose tissue (arrows). **Figure 2** Mammary gland - Fibrosis in a male F344/N rat from a chronic study (higher magnification of Figure 1). Mature fibrous connective tissue surrounds a mammary gland duct and alveoli and extends into the adjacent mammary adipose tissue.

Figure 3 Mammary gland - Fibrosis in a female F344/N rat from a chronic study. Diffuse sheets of mature fibrous connective tissue are a feature of concurrent lobular hyperplasia in the mammary gland. **Figure 4** Mammary gland - Fibrosis in a female F344/N rat from a chronic



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study (higher magnification of Figure 3). A diffuse sheet of mature fibrous connective tissue surrounds mammary gland ducts and alveoli.

Keywords: mouse; rat; mammary gland; fibrosis; stroma; periductular

Comment: Variable degrees of fibrosis of the mammary gland lobule are commonly seen in older rats and mice. Mammary gland fibrosis is usually periductular and often occurs secondary to other changes, such as cystic ductal dilation, galactoceles, chronic inflammation, atrophy, epithelial hyperplasia, and neoplasia. However, mammary gland fibrosis can also be a primary change due to experimental manipulations or chemical exposures, such as implantation of foreign materials, iodine deficiency, or prenatal exposure to organochlorines in rats. It can also be associated with the proliferation of small- and medium-sized ducts in BALB/c mice treated with epidermal growth factor. Mammary gland fibrosis is characterized by increased amounts of mature fibrous connective tissue surrounding mammary gland ducts (periductular) and extending into the adjacent mammary adipose tissue (Figure 1 and Figure 2). Diffuse sheets of mature fibrous connective tissue are a feature of lobular hyperplasia (Figure 3 and Figure 4). Fibrosis must be differentiated from early fibroadenomas, which are nodular, space-occupying lesions.

Recommendation: Mammary gland fibrosis should be diagnosed and assigned a severity grade if it is a primary change. Fibrosis occurring as a secondary change to other lesions (such as duct dilatation, galactocele, inflammation, epithelial hyperplasia, neoplasia, etc.) should not be diagnosed separately unless warranted by severity, though it should be described in the pathology narrative.

References:

Boorman GA, Wilson JT, van Zwieten M, Eustis SL. 1990. Mammary gland. In: Boorman GA, Eustis SL, Elwell MR, Montgomery CA, Mackenzie WF (eds.). 2016. Pathology of the Fischer rat: reference and atlas. Academic Press pp. 295-313.

Devor DE, Waalkes MP, Goering P, Rehm S. 1993. Development of an animal model for testing human breast implantation materials. *Toxicol Pathol* 21(3):261-73.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/8248715>



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El Sheikh Saad H, Meduri G, Phrakonkham P, Berges R, Vacher S, Djallali M, Auger J, Canivenc-Lavier MC, Perrot-Appanat M. 2011. Abnormal peripubertal development of the rat mammary gland following exposure in utero and during lactation to a mixture of genistein and the food contaminant vinclozolin. *Repro Toxicol* 32(1):15-25.

Abstract: <https://pubmed.ncbi.nlm.nih.gov/21539910>

Eskin BA, Grotkowski CE, Connolly CP, Ghent WR. 1995. Different tissue responses for iodine and iodide in rat thyroid and mammary glands. *Biol Trace Element Res* 49(1):9-19.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/7577324>

Foster WG, Younglai EV, Boutross-Tadross O, Hughes CL, Wade MG. 2004. Mammary gland morphology in Sprague-Dawley rats following treatment with an organochlorine mixture in utero and neonatal genistein. *Toxicol Sci* 77(1):91-100.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/14514955>

Greaves P. 2007. Mammary gland. *Histopathology of preclinical toxicity studies: interpretation and relevance in drug safety evaluation*, 3rd ed. Academic Press. pp. 69-98.

McMartin DN, Sahota PS, Gunson DE, Hsu HH, Spaet RH. 1992. Neoplasms and related proliferative lesions in control Sprague-Dawley rats from carcinogenicity studies. Historical data and diagnostic considerations. *Toxicol Pathol* 20(2):212-25.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/1475582>

Molinolo A, Simian M, Vanzulli S, Pazos P, Lamb C, Montecchia F, Lanari C. 1998. Involvement of EGF in medroxyprogesterone acetate (MPA)-induced mammary gland hyperplasia and its role in MPA-induced mammary tumors in BALB/c mice. *Cancer Lett* 126(1): 49-57.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/9563648>

Seely JC, Boorman, GA. 1999. Mammary gland and specialized sebaceous glands. In: Maronpot RR, Boorman GA, Gaul BW (eds.). 1999. *Pathology of the mouse: reference and atlas*. Cache River Press pp. 613-35.

Van Zwieten MJ, HogenEsch H, Majka JA, Boorman GA. Nonneoplastic and neoplastic lesions of the mammary gland. In: Mohr U, Dungworth DL, Capen CC (eds.). 1994. *Pathobiology of the Aging Rat*, Vol. 2. International Life Sciences Press pp. 459-474.

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