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Atrophy, acinar cell

Pathogenesis:

Decrease in number and/or size of acinar cells may be due to spontaneous or experimentally induced degenerative changes, apoptosis, or a sequel of chronic inflammation.

Diagnostic key features:

- Focal, lobular, or diffuse.
- Reduction in the number and/or size of acini.
- Loss of acinar cell basophilia and decreased zymogen granules.
- Relatively prominent intra and inter-lobular ducts.
- Variably dilated cyst-like or duct-like acini and/or ducts lined by cuboidal or flattened epithelial cells.
- Transitional structures containing mixtures of normal acinar cells, atrophic acinar cells, and cuboidal ductal cells.

Pancreas

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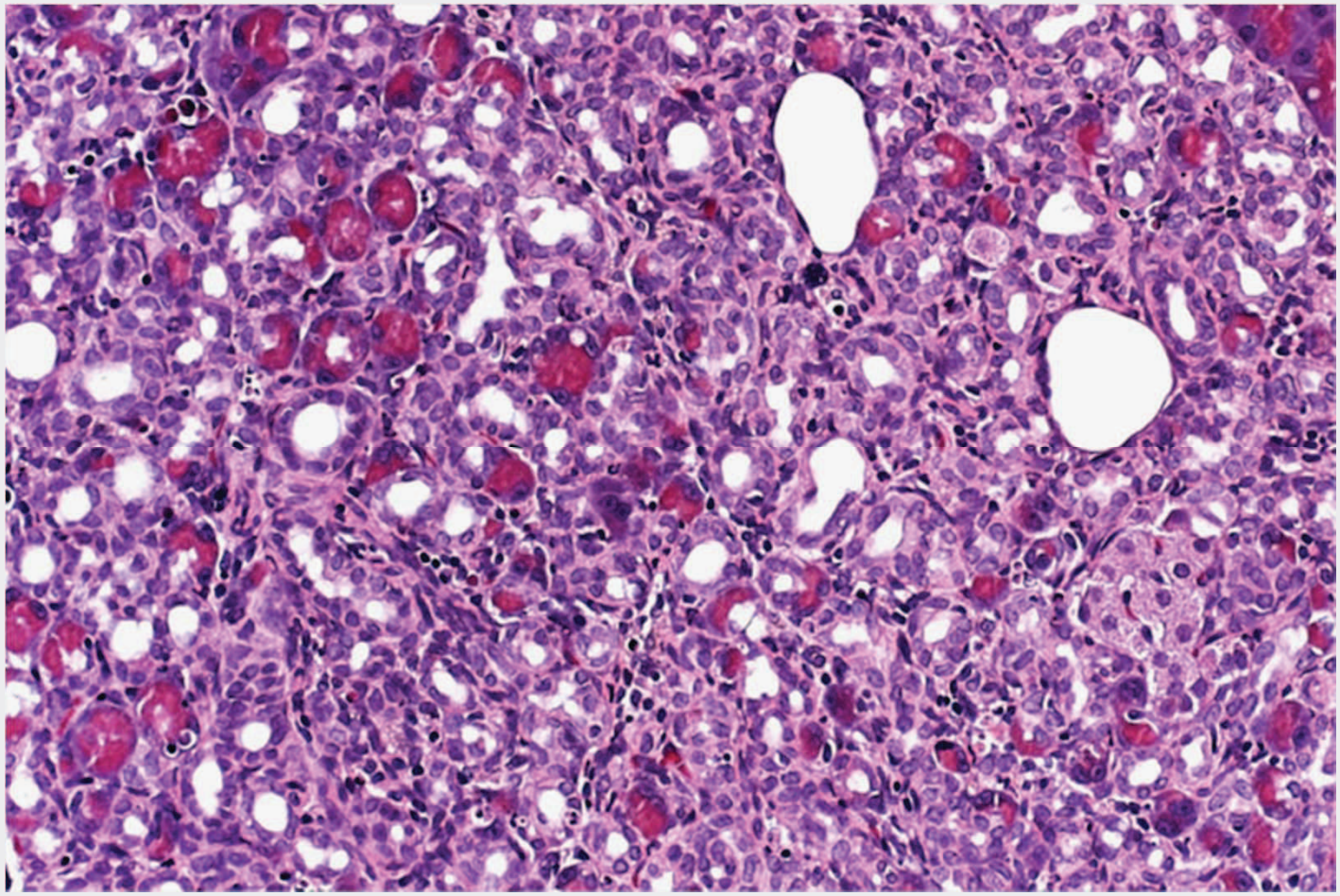
Atrophy, acinar cell



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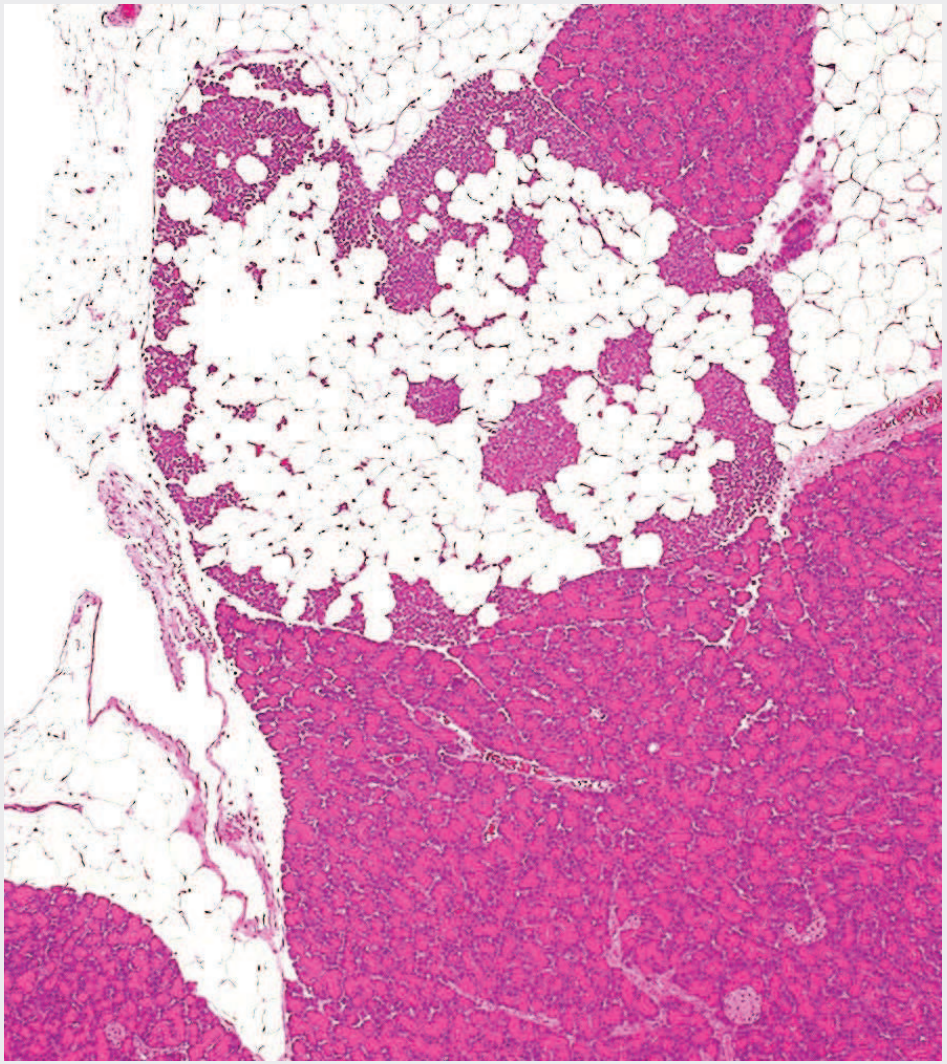
Atrophy, acinar cell



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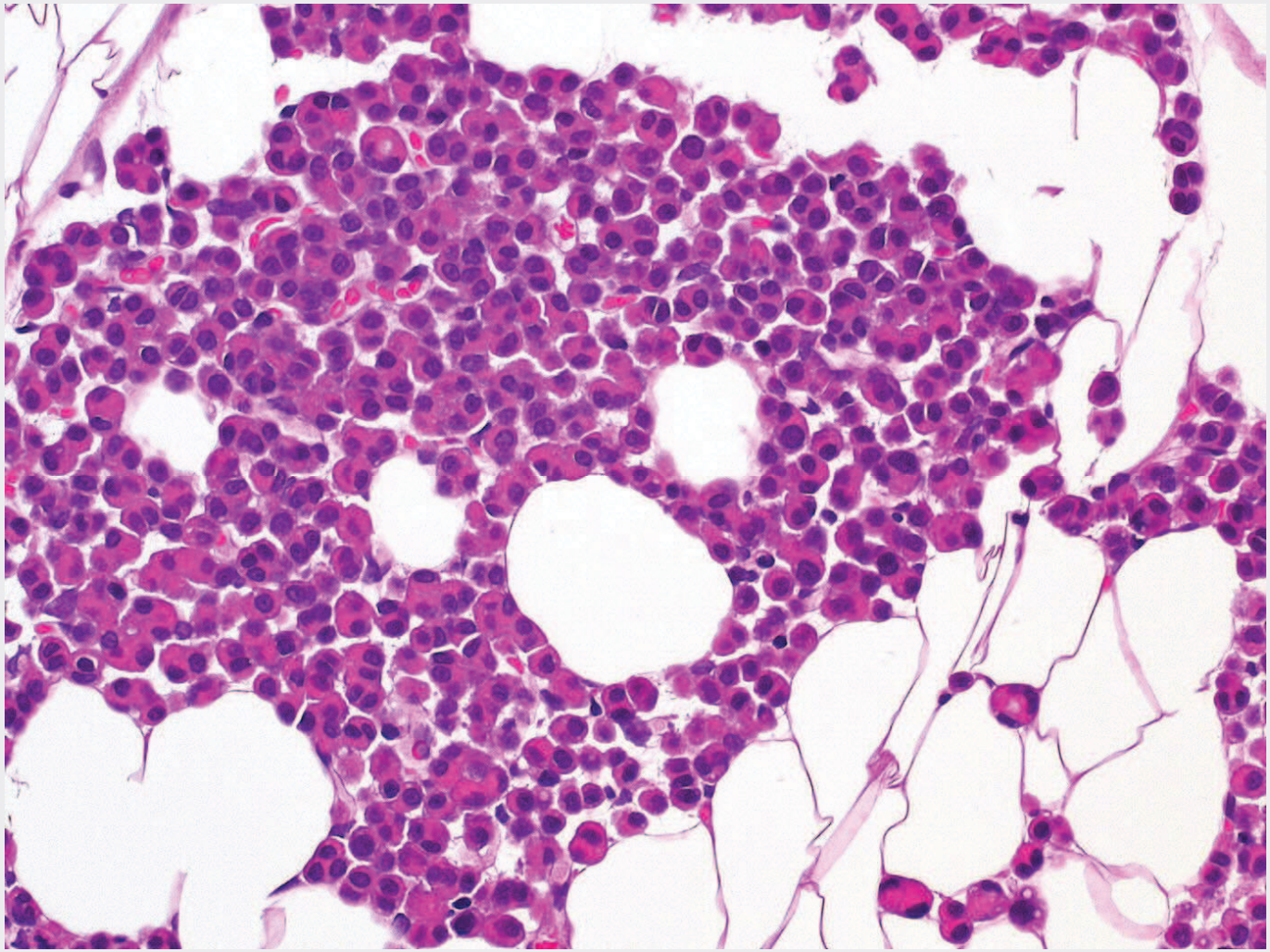
Atrophy, acinar cell



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Atrophy, acinar cell

Differential diagnoses:

Secretory depletion, acinar cell:
Diffuse reduction of zymogen granules but maintenance of the basophilic basal cytoplasm; no fibrosis or adipocyte infiltration.

Peri-insular halos:
Tele-insular acinar cells have relatively less zymogen granules and more RER when compared to peri-insular acinar cells. In certain planes of section, areas with more teleinsular halos may give a false impression of atrophy.

Metaplasia, ductular:
Progression of ductular metaplasia to ductular hyperplasia and neoplasia.

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Metaplasia, ductular

Synonym: Tubular complexes

Pathogenesis: Acinar cells transdifferentiate or take the appearance of ducts especially in areas of chronic pancreatitis.

Diagnostic features:

- Focal, circumscribed lesions surrounded by normal exocrine acini.
- Variable caliber ductules lined by flat cuboidal epithelial cells.
- Located in the acinar compartment rather than in the native ducts.
- Intermixed with pale atrophic exocrine acini.
- Islets not usually involved.

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Metaplasia, ductular

Comment:

Exocrine acinar ductular metaplasia is usually secondary to chronic pancreatitis and atrophy and is considered a **reparative process**. The diagnosis of ductular metaplasia is not commonly used in toxicologic studies since it is one of the features of atrophy.

In DMBA implantation studies in rats that resulted in pancreatic ductular adenocarcinoma, these lesions were considered preneoplastic, however, in majority of cases these lesions do not progress to neoplasia. **The diagnosis of ductular metaplasia may be considered in those studies where a progression to ductular hyperplasia and neoplasia is noted.**

Differential diagnoses:

Hyperplasia, Ductular:
Does not have intermixed pale exocrine acini.

Atrophy, acinar cell:
Ductular metaplasia may be a component in some cases of atrophy and is considered a reparative process; no progression to ductular hyperplasia and neoplasia.

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Tumor, mixed, malignant

Histogenesis: Glandular epithelial and myoepithelial / mesenchymal cells.

Diagnostic features:

- Features of both a sarcoma and a carcinoma are present.
- Cellular and nuclear pleomorphism.
- Invasion is present.

Differential diagnoses

- Tumor, mixed, benign: Features of both a benign mesenchymal tumor and an adenoma; no cellular pleomorphism, no local invasion.
- Myoepithelioma, malignant: Tumor cells with epithelioid differentiation or palisading around blood vessels; areas of densely packed elongated to spindeloid tumor cells, separated by a delicate and inactive tumor stroma.

Salivary glands

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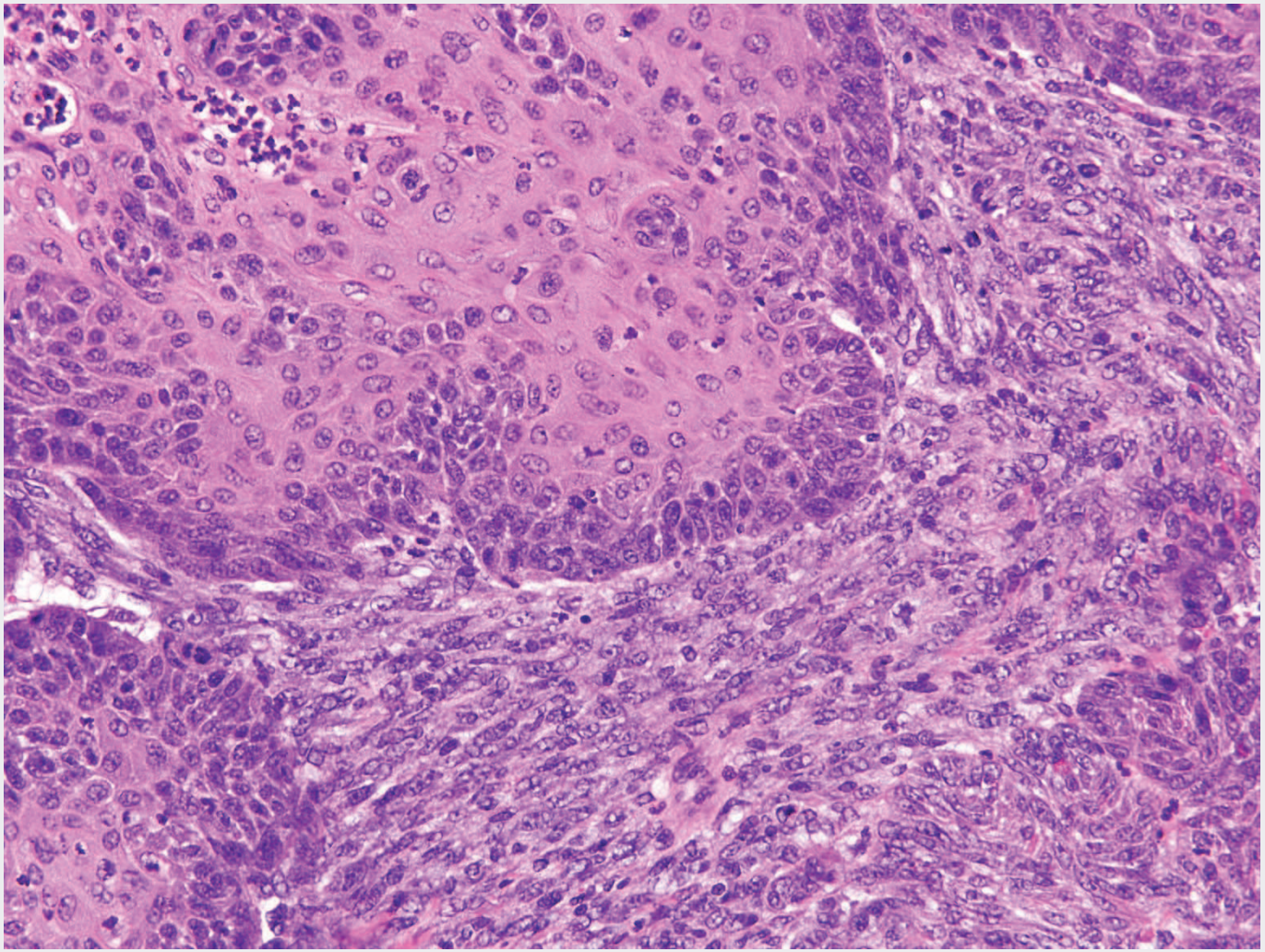
Tumor, mixed, malignant



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Boehringer Ingelheim

Myoepithelioma, malignant

Histogenesis: Myoepithelial cells, extraglandular ductal origin, salivary glands (possibly other glandular tissues).

Diagnostic key features:

- Mixed tumor morphology with confluent regions of basal, stratified squamous, and spindle cell patterns; may contain tubular structures adjacent to blood vessels, tumor cells may show palisading basal cell pattern or align in epithelioid fashion.
- Squamous appearance without keratinization or pearl formation may occur in some areas.
- Invasion into surrounding tissue or vessels may be present; large tumors may metastasize to the lung.
- Infiltrates of lymphocytes and plasma cells are not present (unlike polyoma virus neoplasms).

Salivary glands

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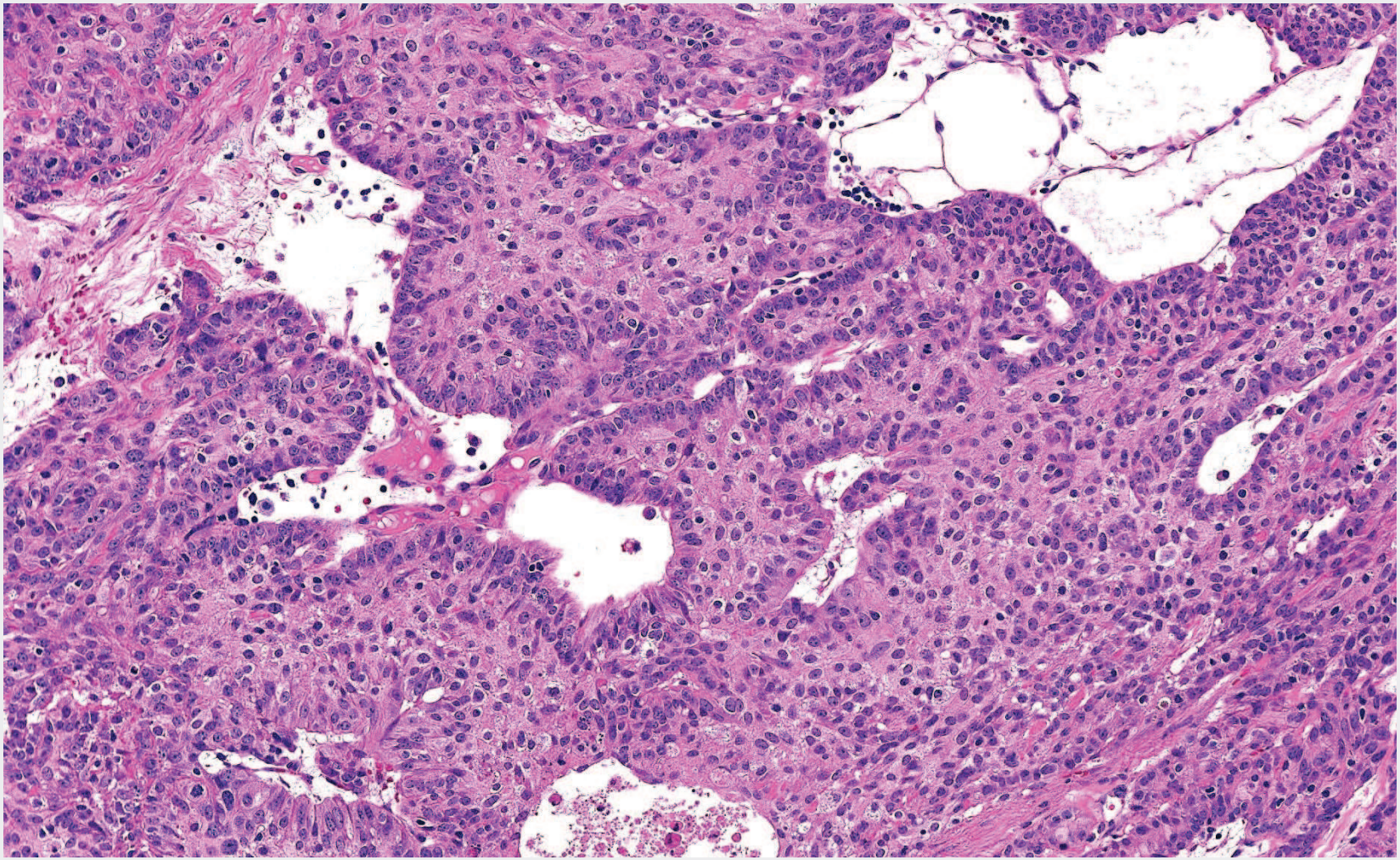
Myoepithelioma, malignant



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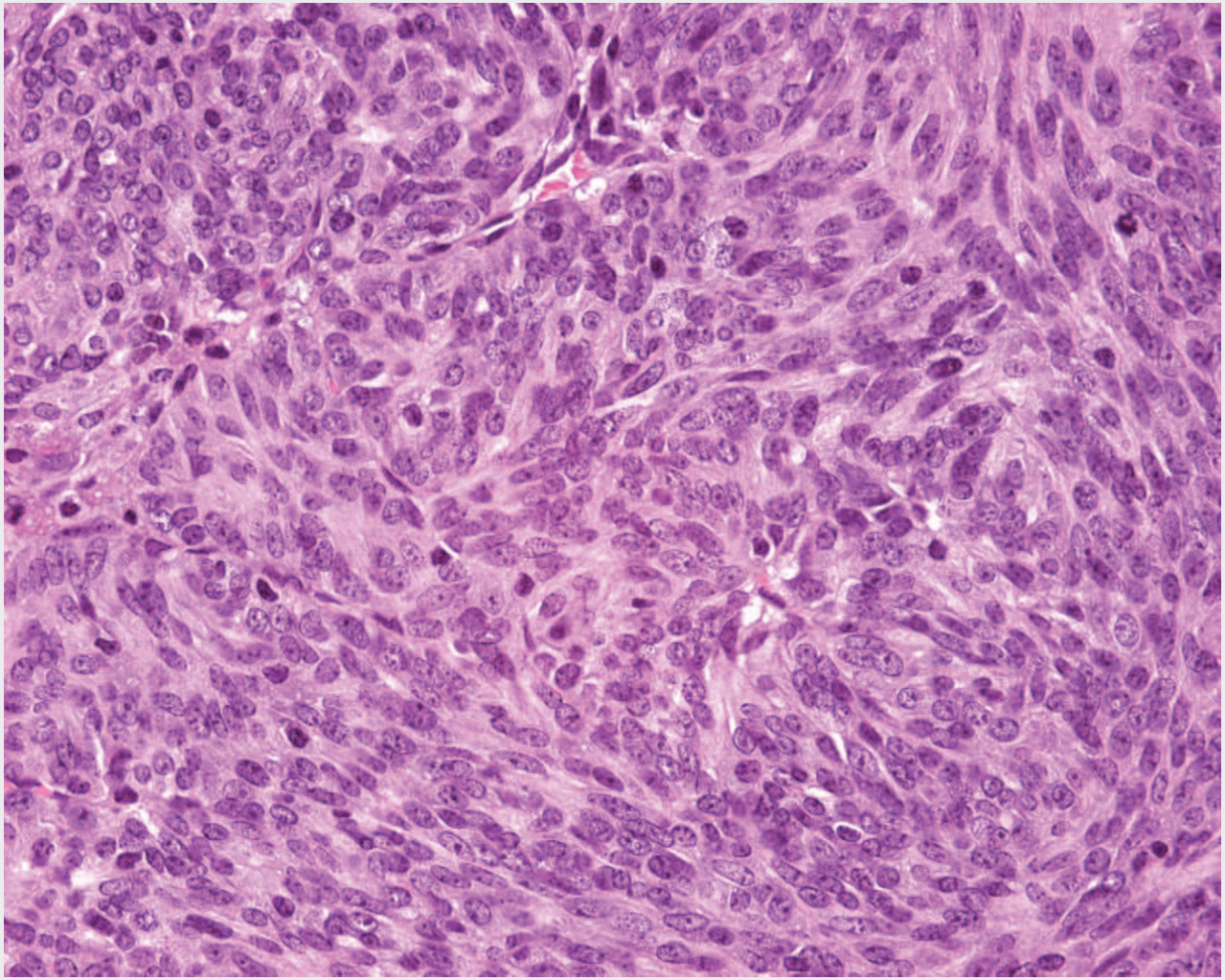
Salivary glands

Myoepithelioma, malignant



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Myoepithelioma, malignant

Histogenesis: Myoepithelial cells, extraglandular ductal origin, salivary glands (possibly other glandular tissues).

Comment:

- Have not been described in rats; rare in most strain of mice but occur more often in BALB/c, A/J, and C58 strains (mainly females)
- Occur most frequently in the ventral neck region (parotid and submandibular glands), but may also arise from other glandular tissues, e.g. mammary or extraorbital lacrimal glands
- Stain positive for cytokeratin and vimentin, but negative for α smooth muscle actin, in contrast to normal myoepithelial cells
- Confirmatory immunohistochemistry may be required for differentiation from scirrhous squamous cell carcinomas or mixed malignant tumors

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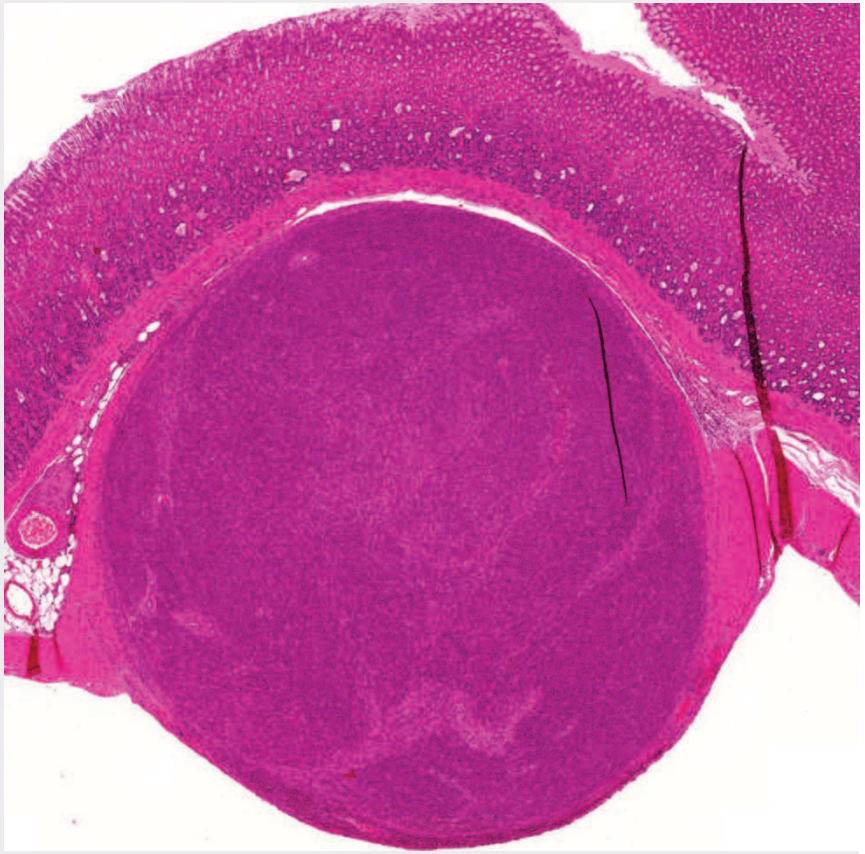
Leiomyoma

Histogenesis: Smooth muscle cells from tunica muscularis

Diagnostic features:

- Intramural involvement.
- Interlacing bundles and whorls of uniform spindle cells arranged in criss-cross patterns of bundles.
- Nuclei typically blunt-ended or cigar shaped.
- Eosinophilic cytoplasm contains longitudinal myofilaments and perinuclear clear spaces and shows immunoreactivity for desmin.



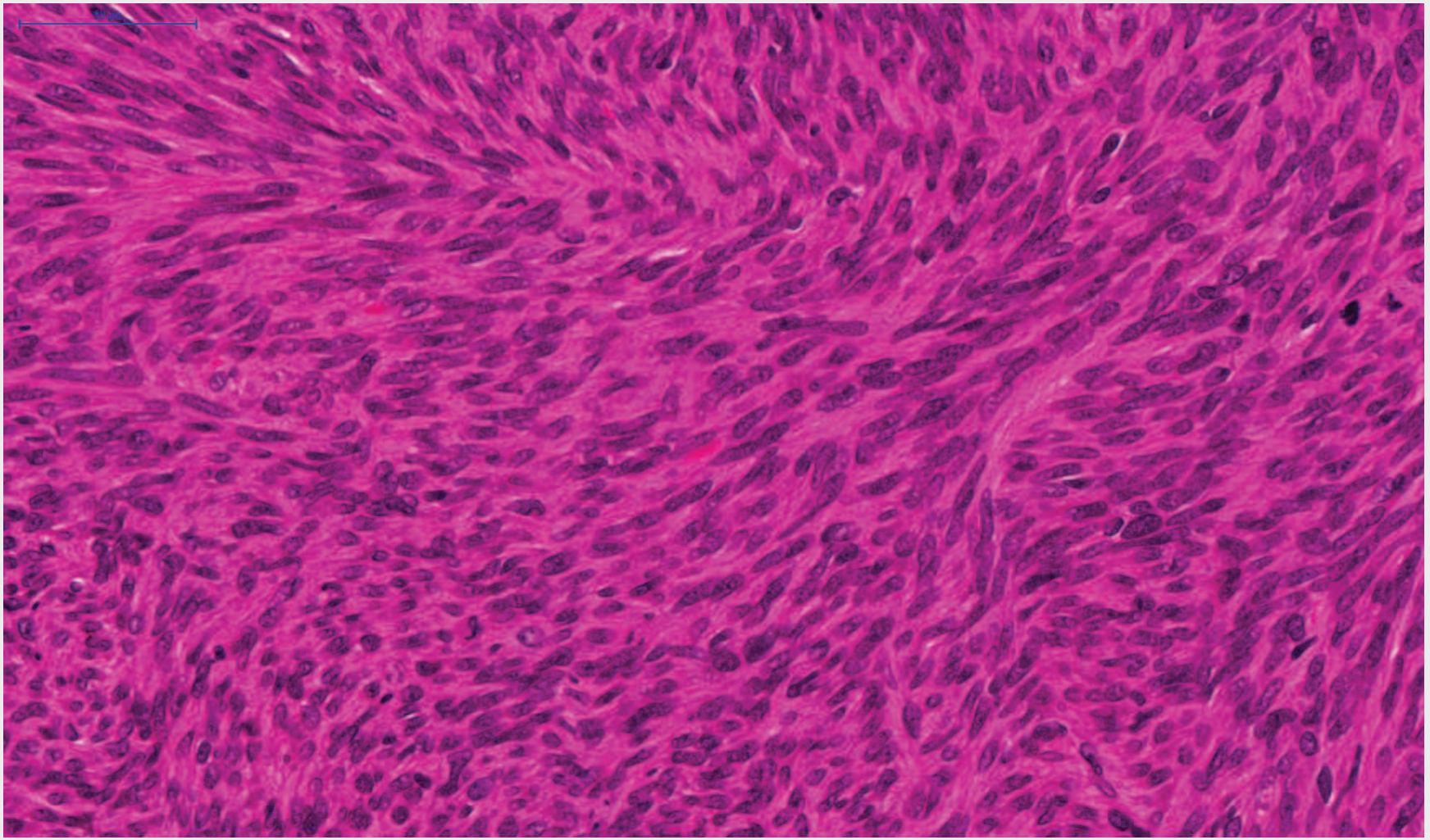
Rat, glandular stomach

Image kindly provided by RITA

Stomach / intestine

Boehringer Ingelheim

Leiomyoma



Rat, glandular stomach

Image kindly provided by RITA

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Gastrointestinal Stromal Tumor (GIST)

Synonyms: Interstitial Cajal cell tumor; gastrointestinal pacemaker cell tumor

Histogenesis: Specialized smooth muscle cells (i.e., interstitial cells of Cajal) in the tunica muscularis or myenteric plexus.

Diagnostic features:

- Benign or malignant phenotype, local infiltration and metastases observed with latter.
- Cells may be arranged in bundles with storiform architecture.
- Spindle, epithelioid, or pleomorphic cell morphology.
- Indistinct cell borders and fibrillary cytoplasm.
- Spindle- or irregular-shaped nuclei.
- Typically CD117 positive (cytokine receptor encoded by c-kit).

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Gastrointestinal Stromal Tumor (GIST)

Differential diagnosis:

Leiomyoma:
CD117 negative, desmin positive; interlacing bundles and whorls of uniform spindle cells arranged in criss-cross pattern; blunt-ended, fusiform nuclei. Minimal nuclear pleomorphism; phosphotungstic acid-hematoxylin positive myofibrils.

Schwannoma:
CD117 negative, S-100 positive; indistinct cell borders, elongate cells with eosinophilic cytoplasm; nuclei sometime arranged in palisades (i.e., Antoni A pattern).

Comment:
GIST will generally not be easily differentiated from leiomyomas / leiomyosarcomas or other soft tissue tumors. However, immunhistochemical differentiation of the different tumor types, including GIST, needs to be performed in case of imbalances in the incidence of smooth muscle tumors in a given study.

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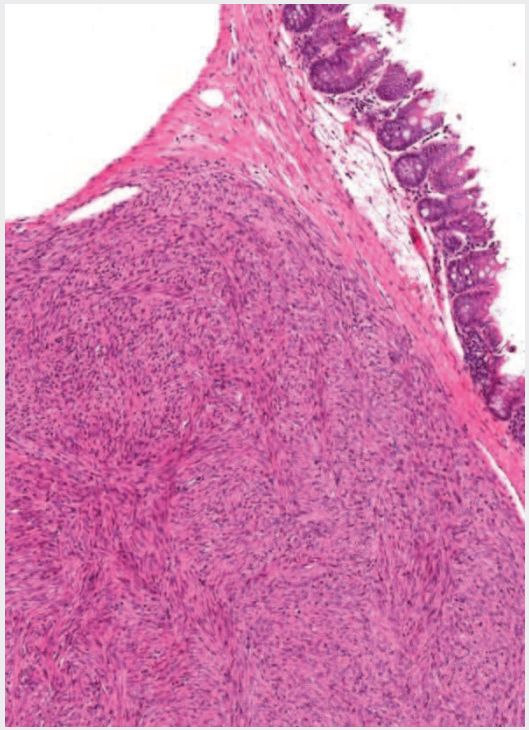
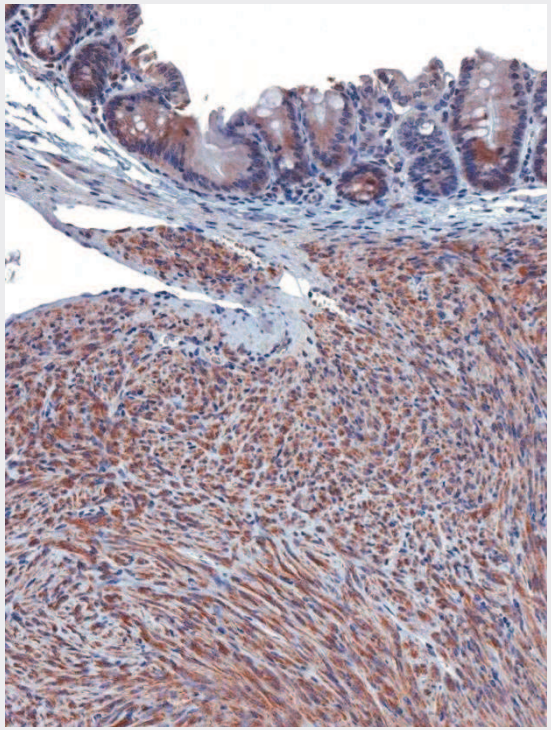
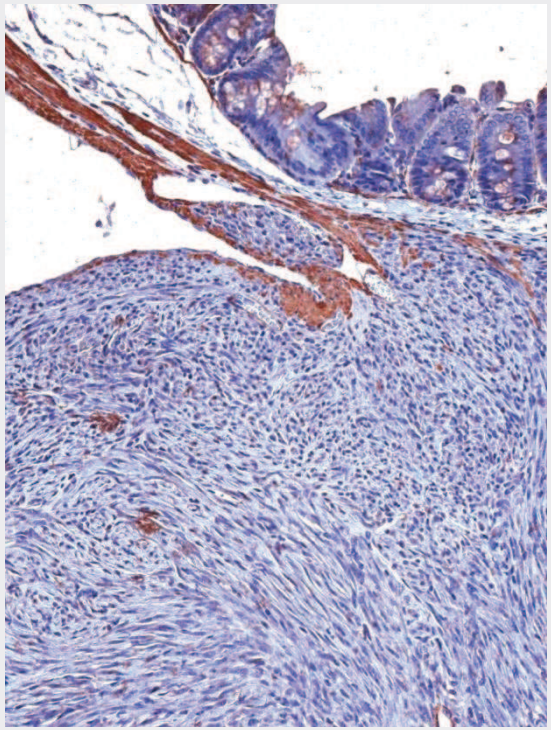
Gastrointestinal Stromal Tumor (GIST)



H&E



CD117



SMA

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INHAND Digestive Tract OWG

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The RITA group

(144 pathologists)