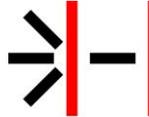


Cutaneous Adnexal Tumors

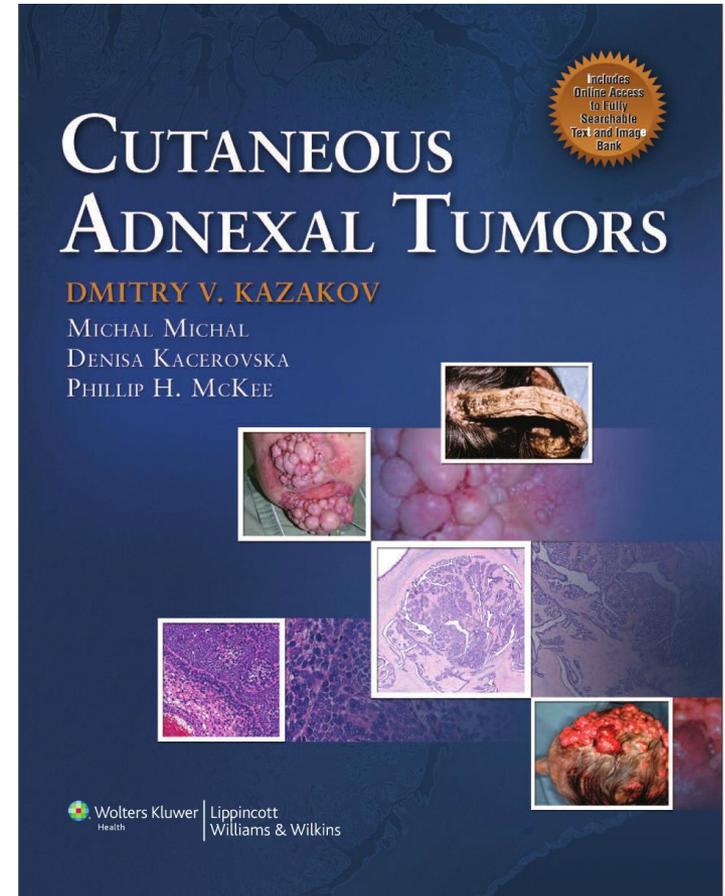
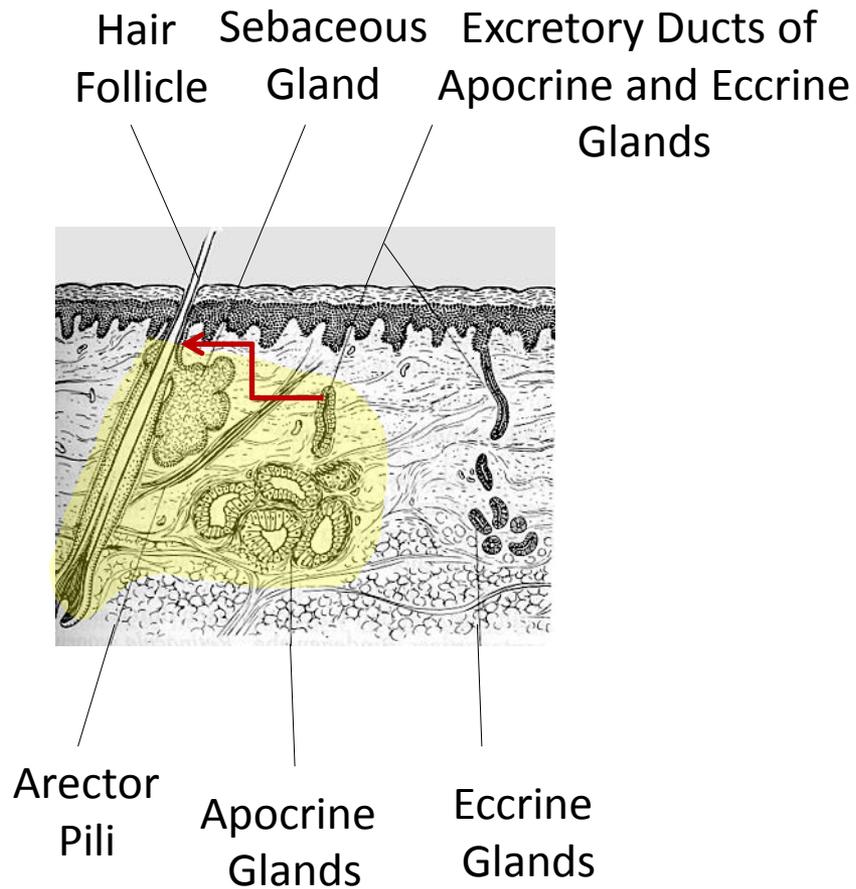
Lesions with Predominant Follicular Differentiation
Special Emphasis on Basal Cell Carcinoma

2014-04-01

Prof. Dr. med. Katharina Glatz
Pathologie

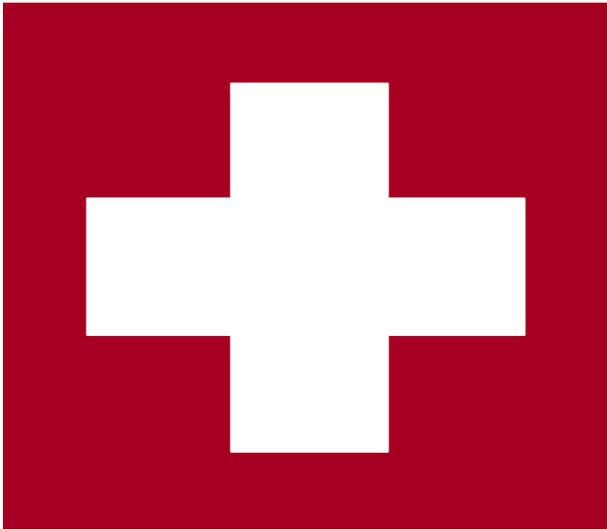
 Universitätsspital
Basel

Cutaneous Adnexal Tumors



Troubling Issues

- **Many synonyms**
- **Published data inaccurate**
- **Criteria for malignancy versus benignancy**
- Eccrine vs. apocrine
- Limited value of IHC
 - Skin adnexal carcinoma: CK5/6+ p63+ D2-40+/-
 - Metastatic adenocarcinoma: CK5/6- p63- D2-40-



Lifetime risk of BCC in Switzerland: 30%
One of the most expensive cancer types!

BASAL CELL CARCINOMA

Histologic Variants of BCC

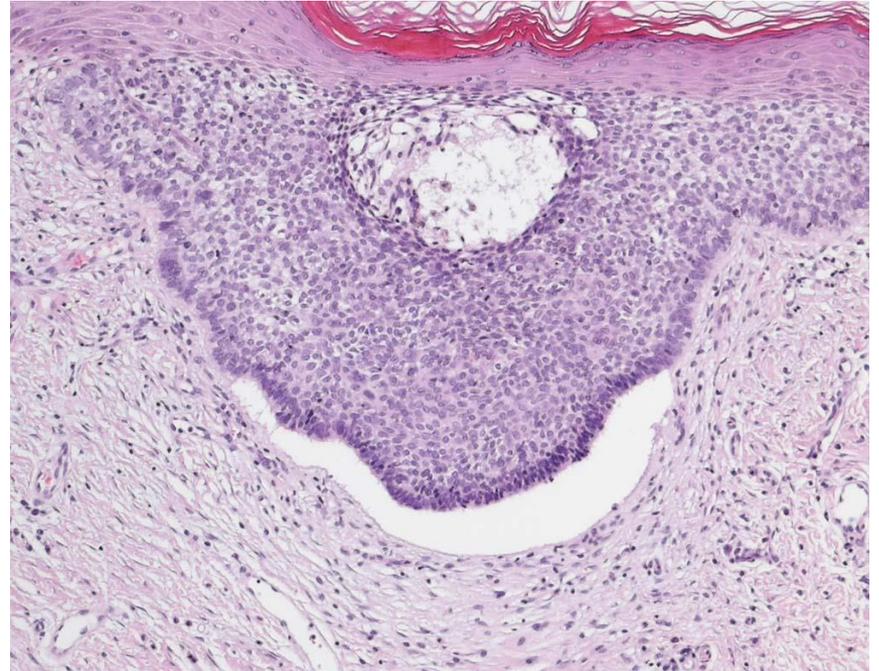
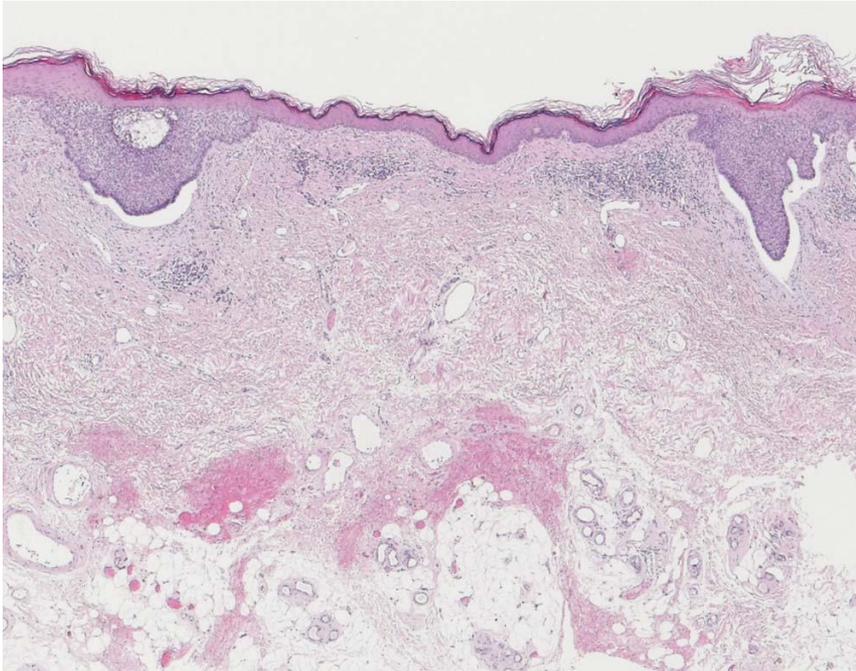
- Adamantinoid
- Apocrine
- Basosquamous
- Cicatrical, keloidal
- Clear cell
- Eccrine
- Fibroepithelioma of Pinkus
- Follicular
- Giant Cell
- Granular cell
- Matrical
- Myoepithelial
- Neuroendocrine differentiation
- Sebaceous
- Signet ring/hyaline inclusion
- Tricholemmal

BCC: Most common subtypes

- Superficial
- Nodular (various subtypes)
- Micronodular
- Infiltrative (non) sclerodermiform

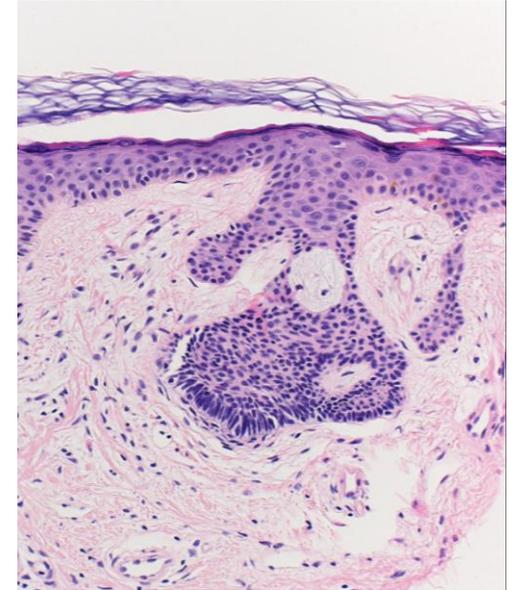
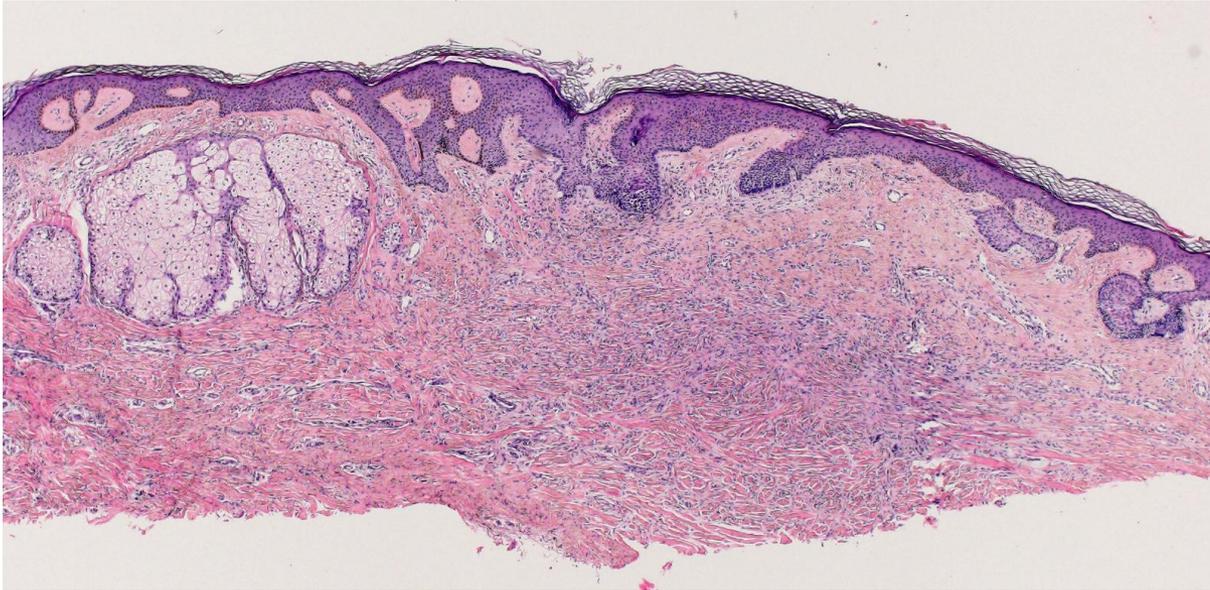
Basaloid skin tumours: Basal cell carcinoma.
Current Diagnostic Pathology 2007; 13:252-272
Carr RA et al.

Superficial BCC



More commonly involving the trunk.
Higher rate of incomplete excision and local recurrence.
Do not involve the reticular dermis. No more than 1mm in thickness.

DD: Hair Follicle Induction in DF

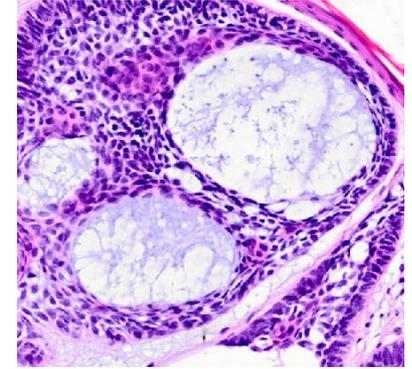
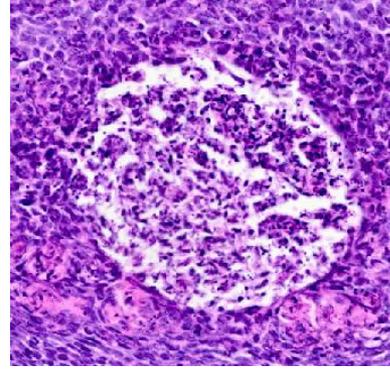
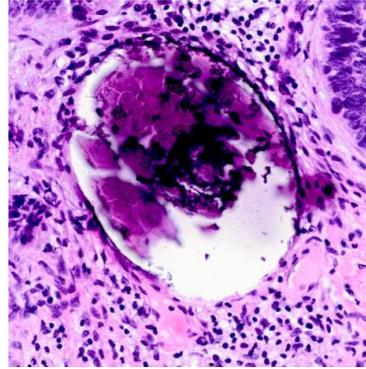
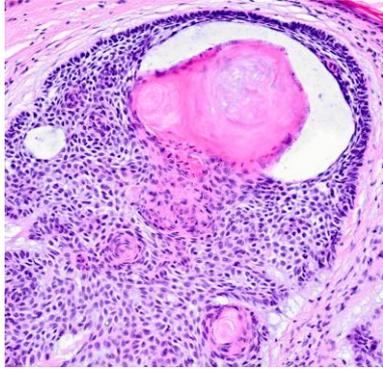


Basaloid follicular hyperplasia or induction of follicles vs. BCC overlying dermatofibroma:

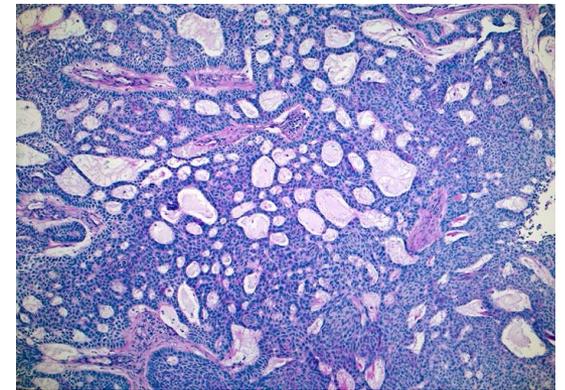
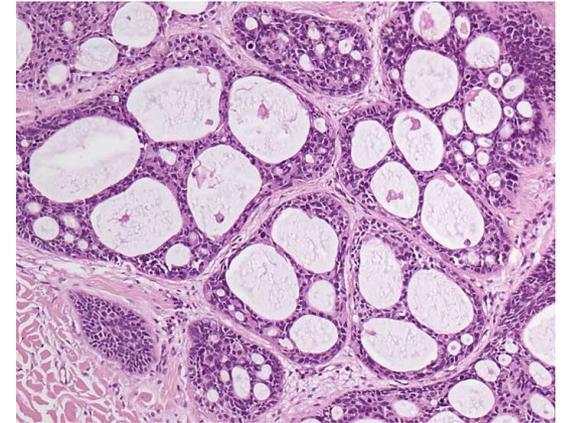
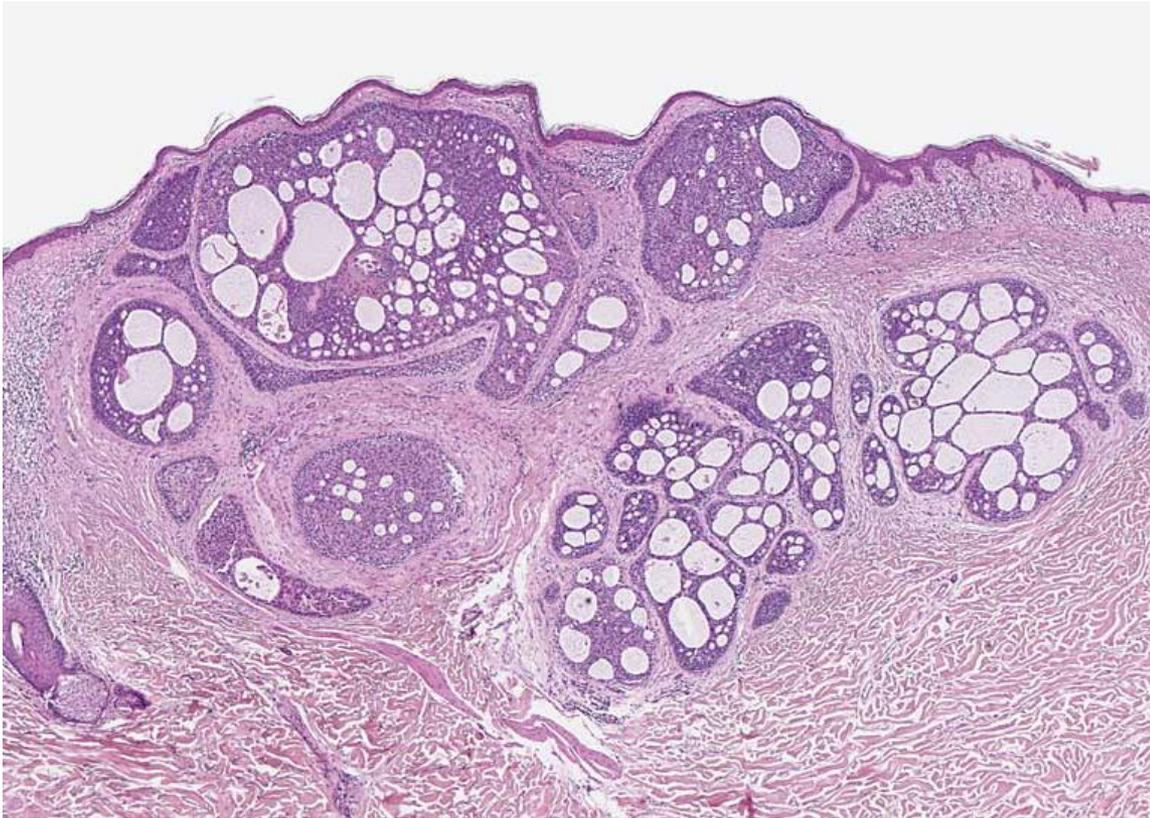
Features supporting diagnosis of BCC:
Prominent retraction artefacts
Large and irregular nests with necroses
High mitotic and apoptotic rate
Lack of papillary mesenchymal bodies
Some cases defy classification!

Basaloid skin tumours:
Mimics of BCC.
Current Diagnostic Pathology
2007; 13:281ff
Carr RA et al.

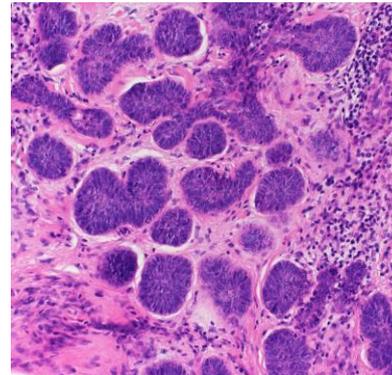
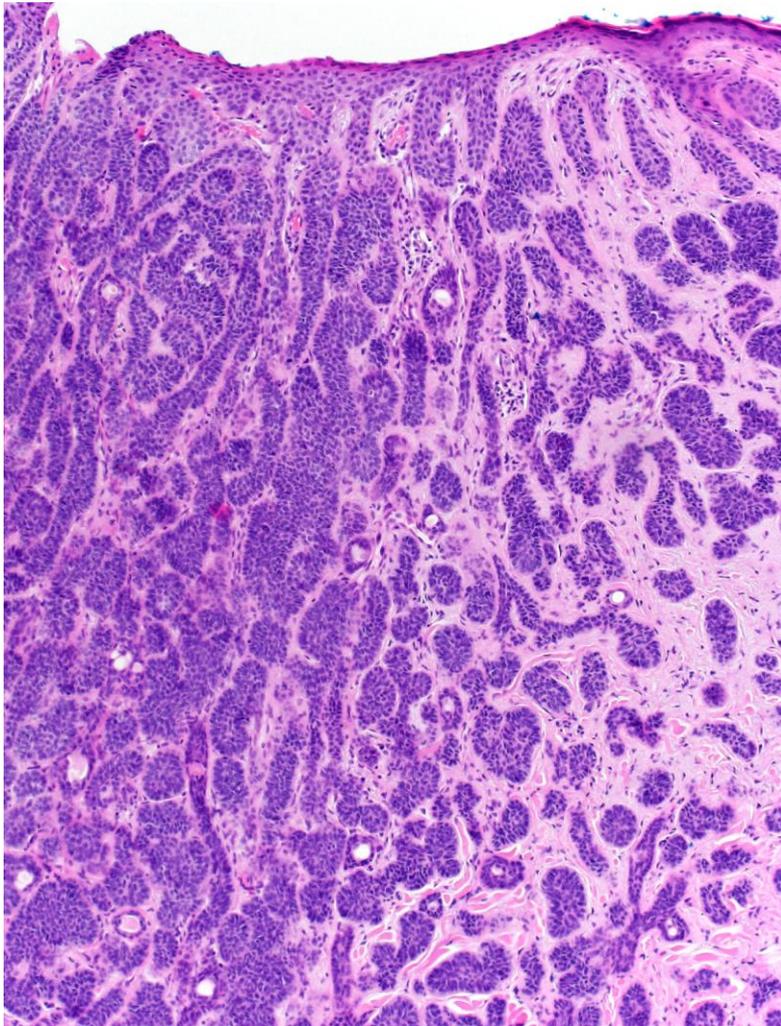
Nodular BCC



Adenoid BCC

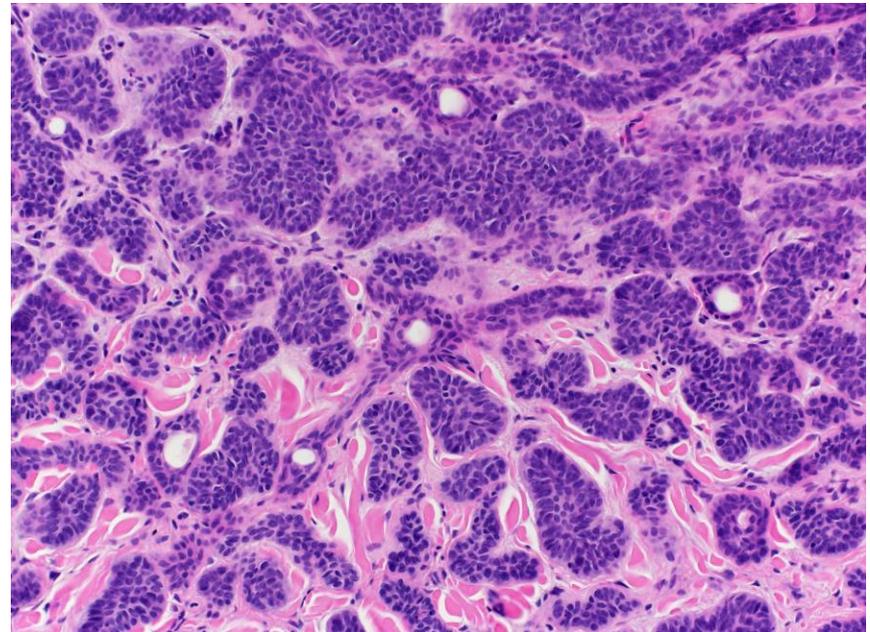


BCC with Ductal Differentiation

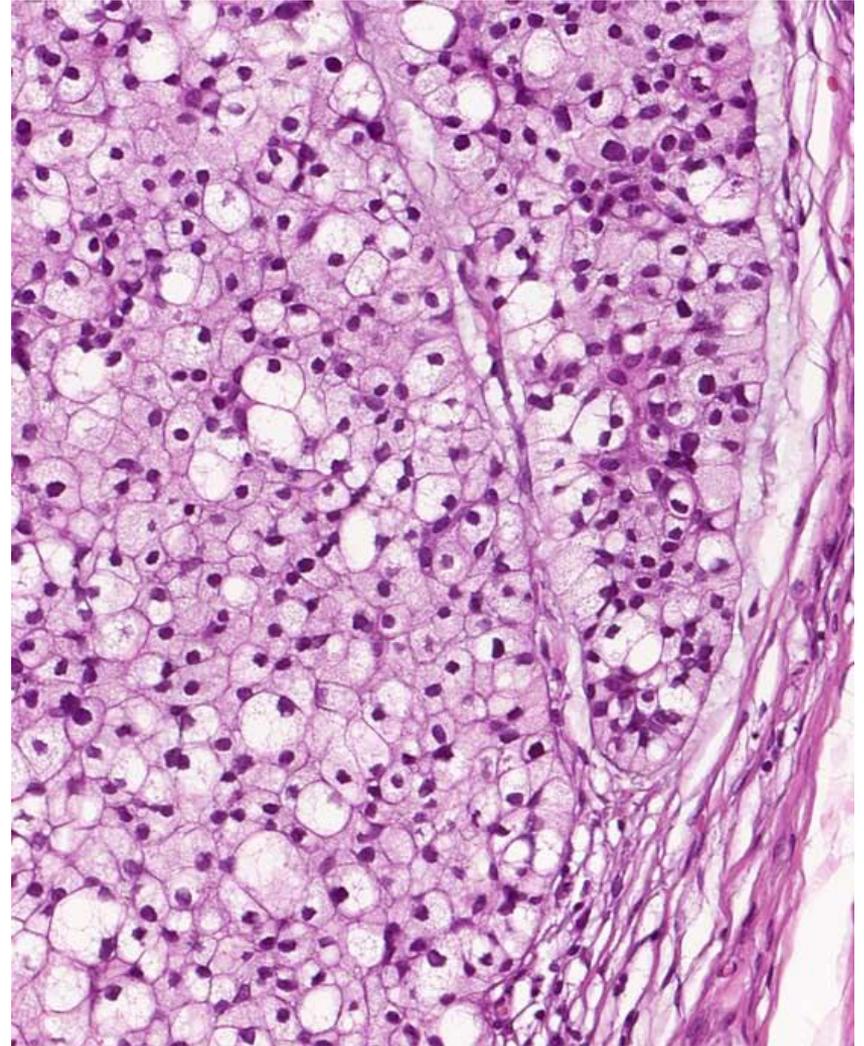
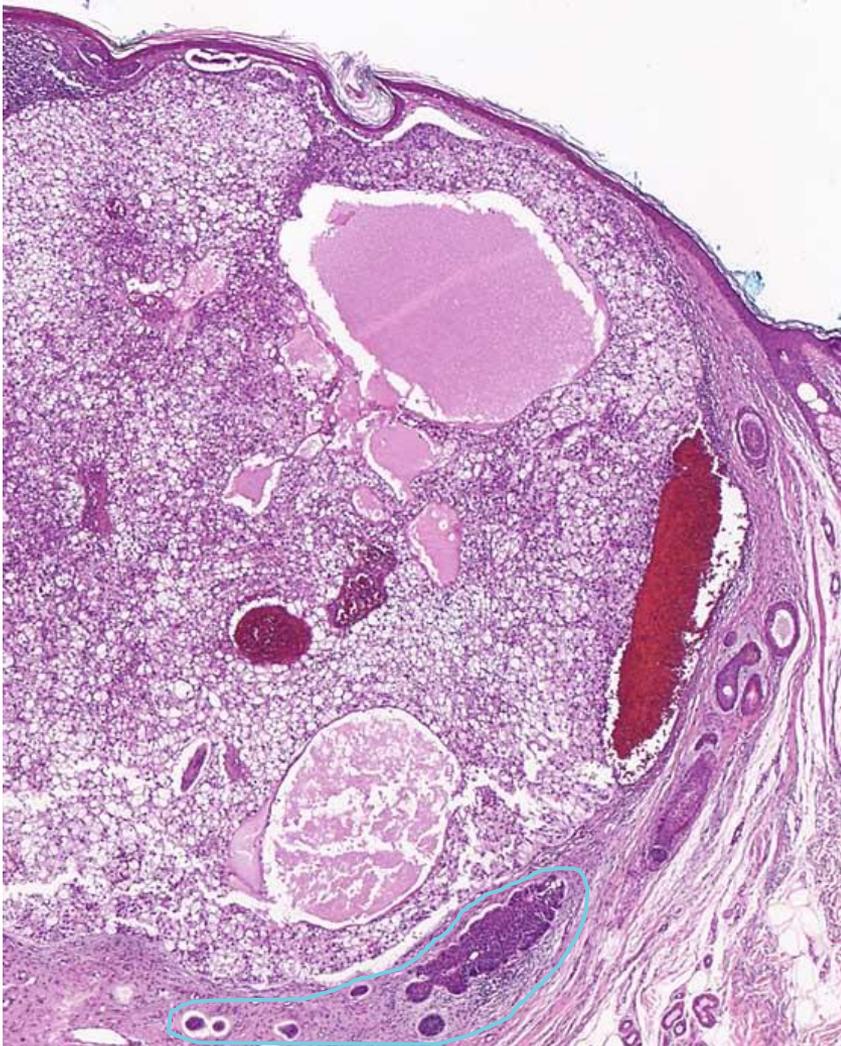


Basal cell carcinoma with unusual
Histologic patterns.
J Am Acad Dermatol 2005; 53:33-837

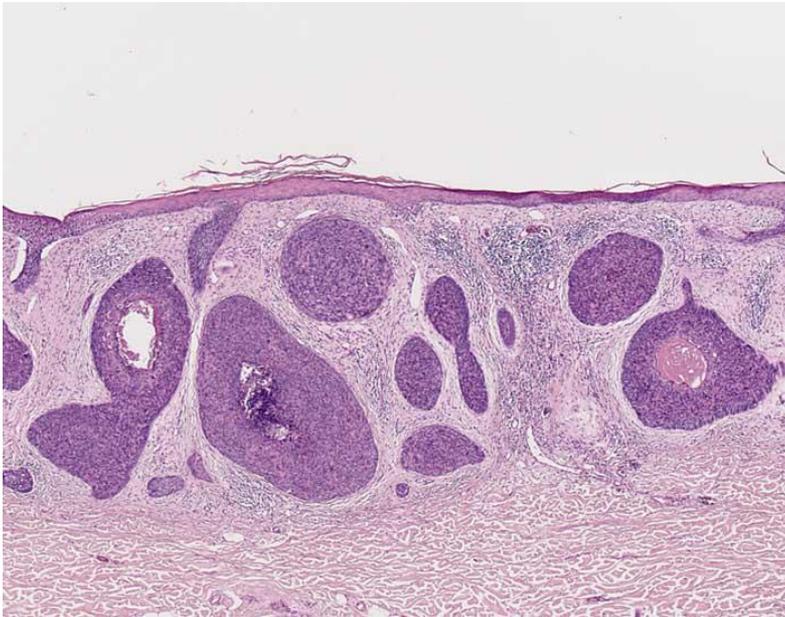
Basal cell carcinoma with ductal
and glandular differentiation.
Eur J Dermatol 2004; 14:383-387



Clear Cell BCC

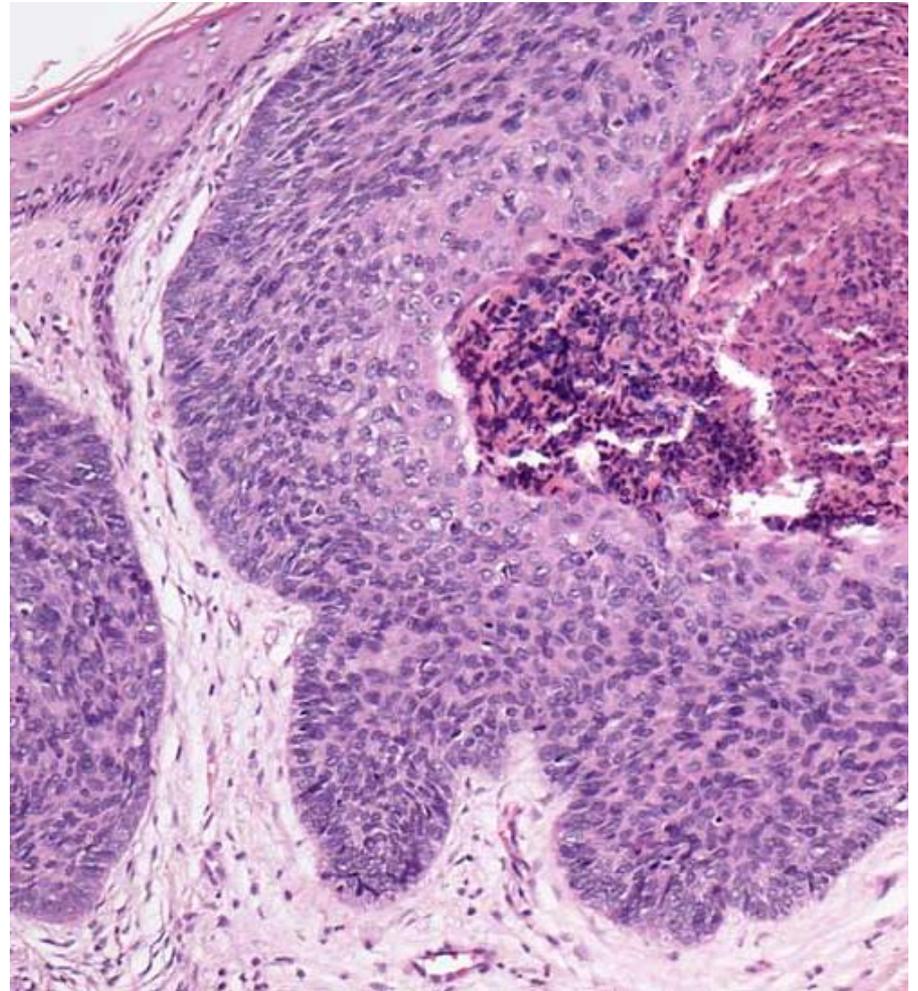


Bowenoid BCC



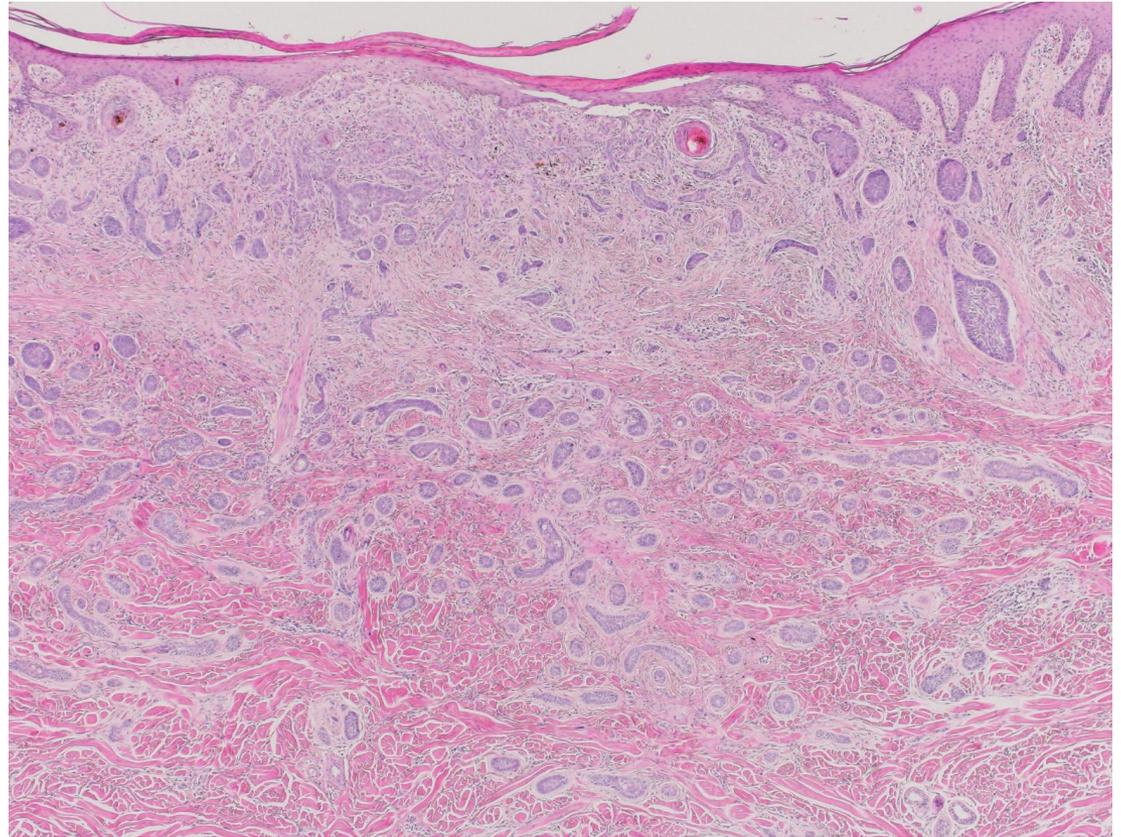
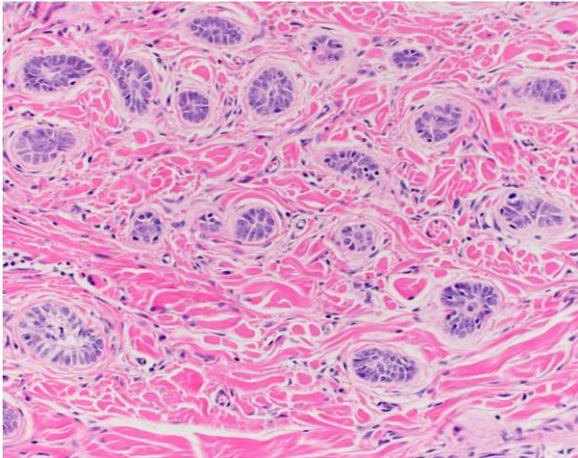
Variant usually of nodular tumors.
Prominent cellular atypia, necroses,
atypical mitoses.

Present clinically as typical BCC and
behave as ordinary BCC.



Micronodular BCC

<25 cells/nodule, <0.15mm
More local recurrence
Penetrate more deeply
Less retraction artefact
Less palisading
Frequent Pn1

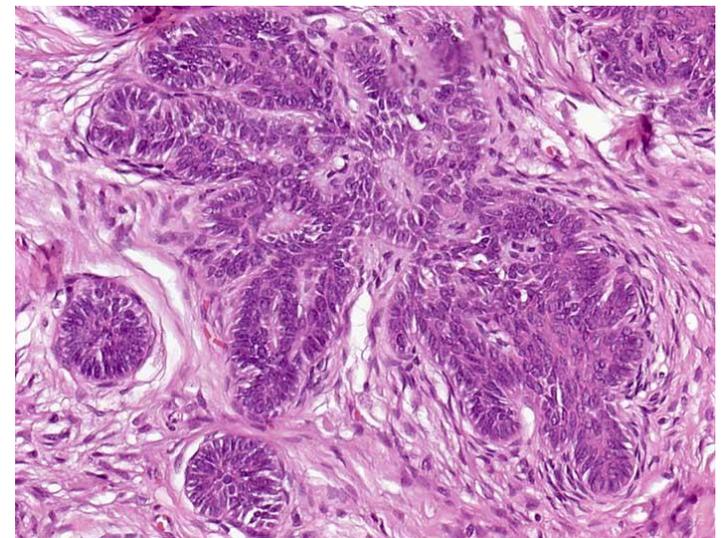
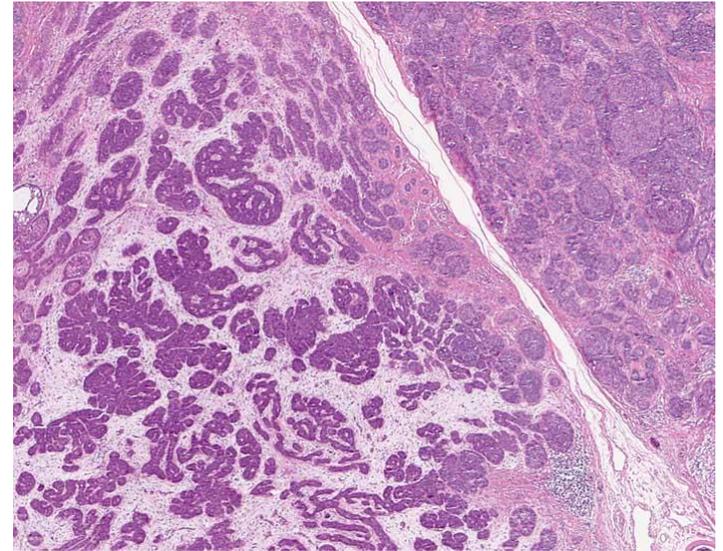
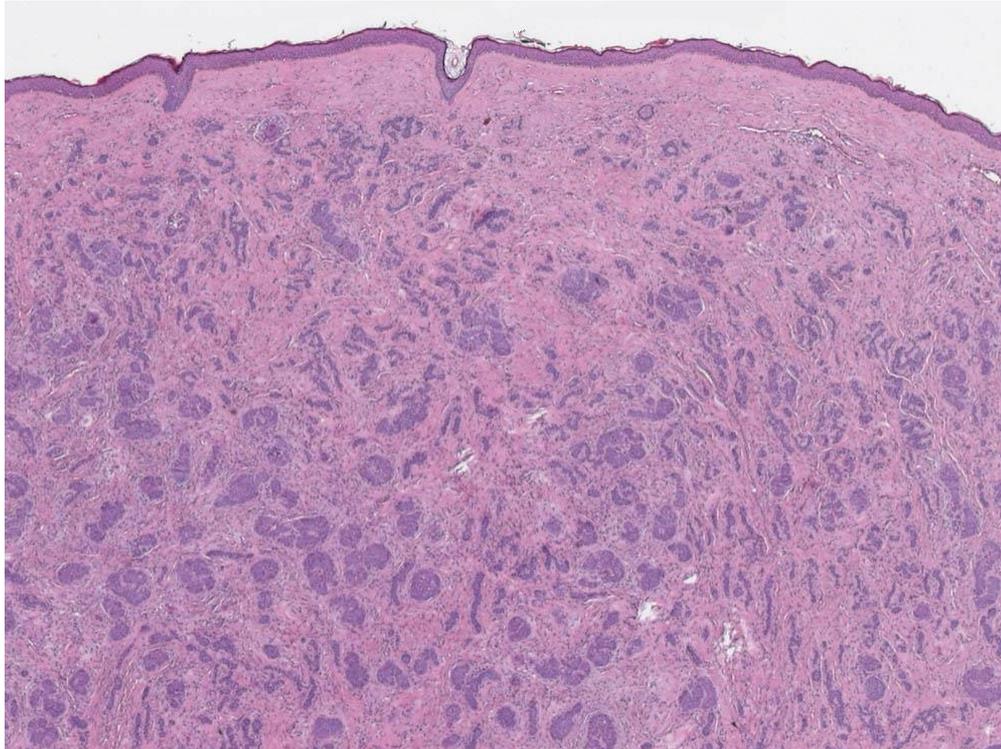


DD: Trichoblastoma

Benign, biphasic epithelial-mesenchymal neoplasm with various growth patterns:

Large nodular, small nodular, retiform, cribriform, racemiform, adamantinoid

DD: Trichoepithelioma, nodular BCC

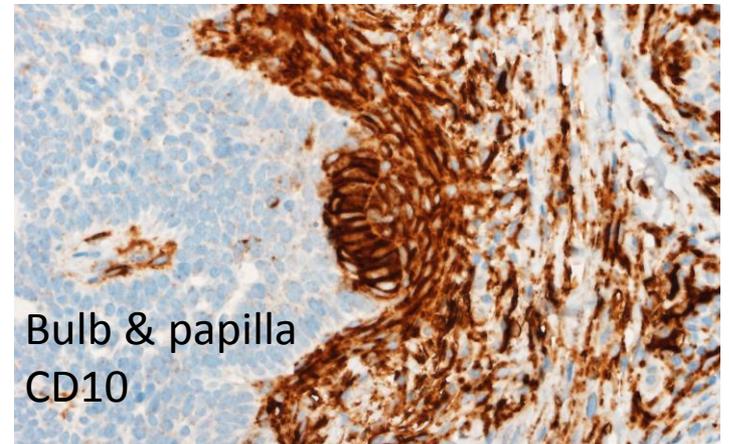
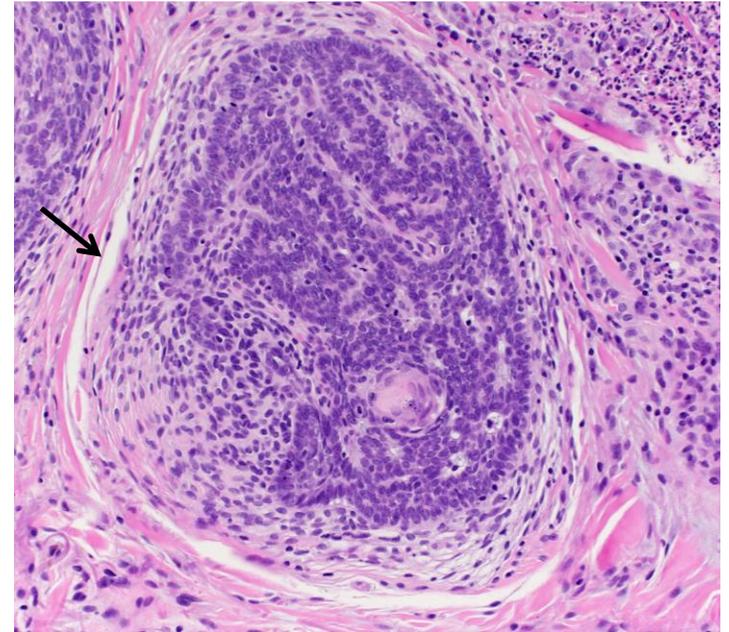
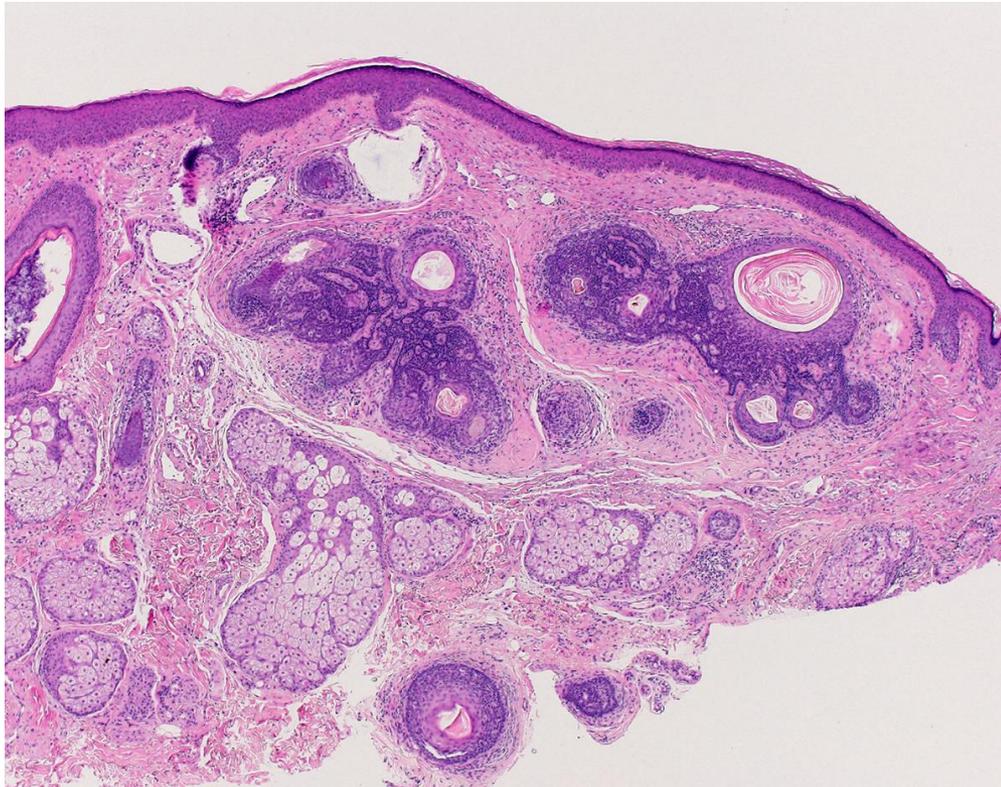


DD: Trichoepithelioma

Trichoepithelioma:

«Superficial trichoblastoma» with prominent superficial follicular differentiation

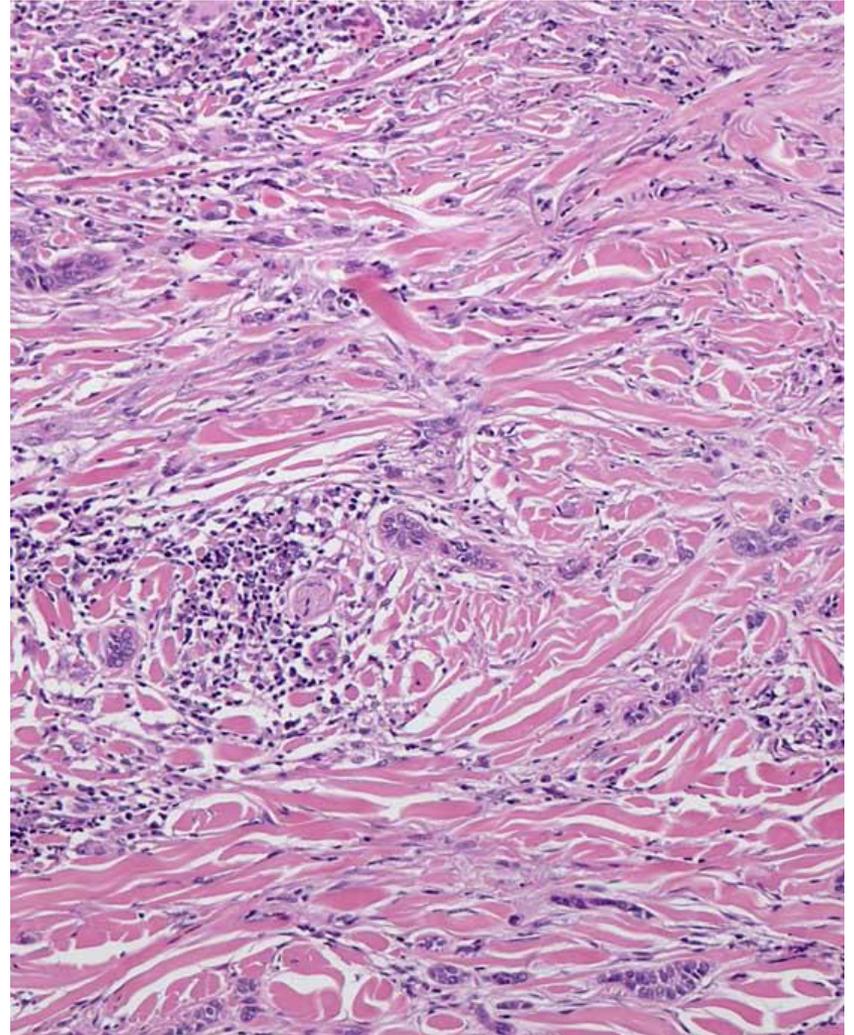
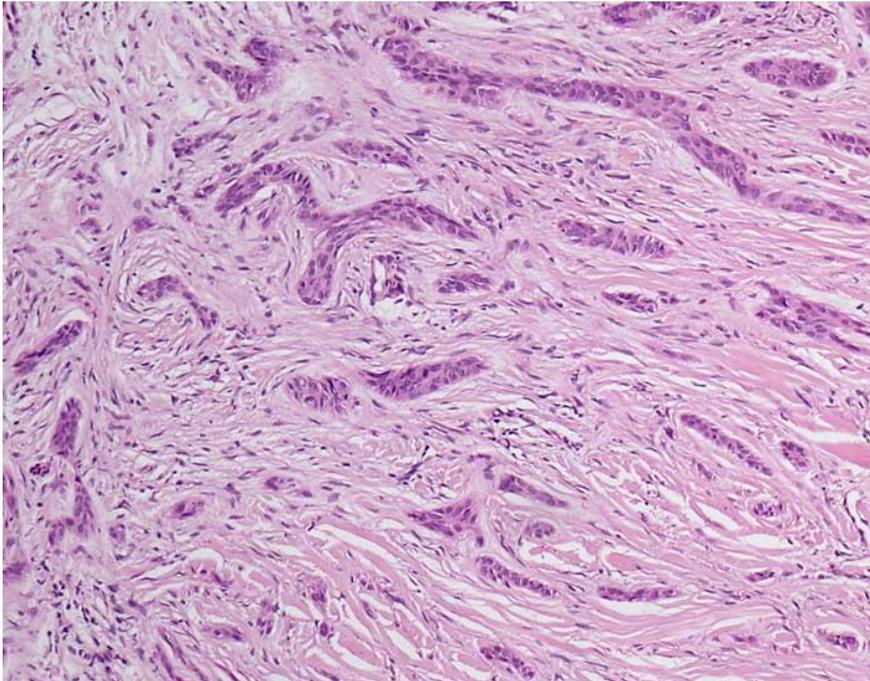
DD: Trichoblastoma, nodular BCC



Infiltrative (Non-) Sclerodermiform

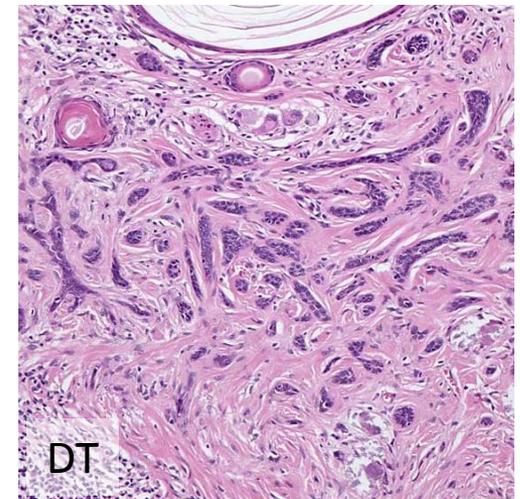
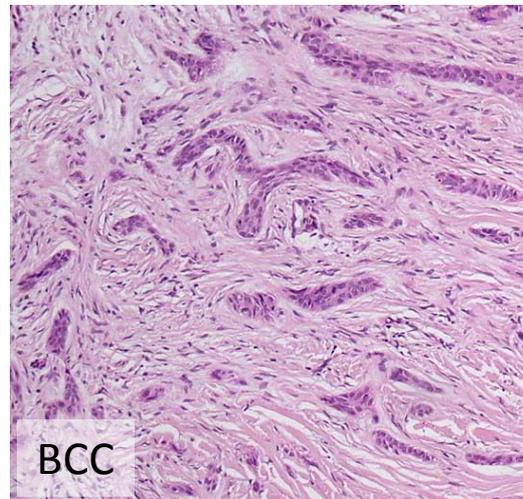
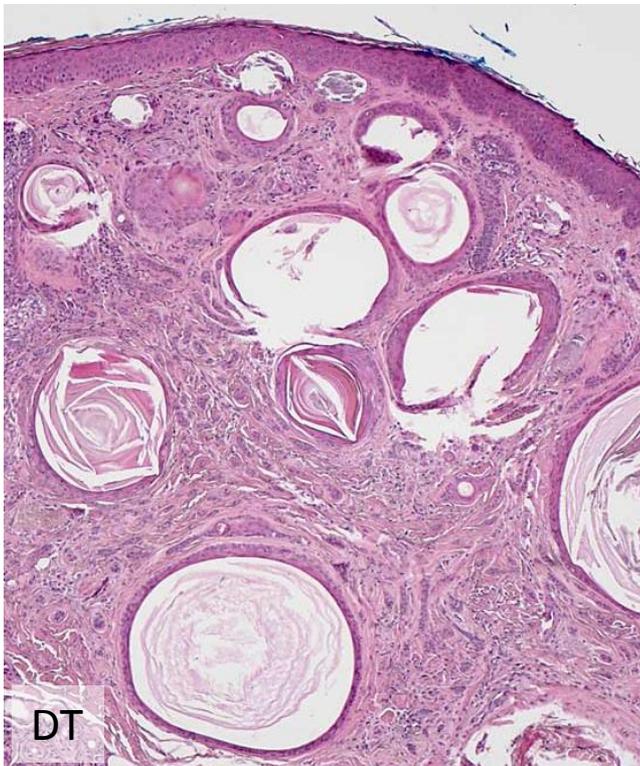
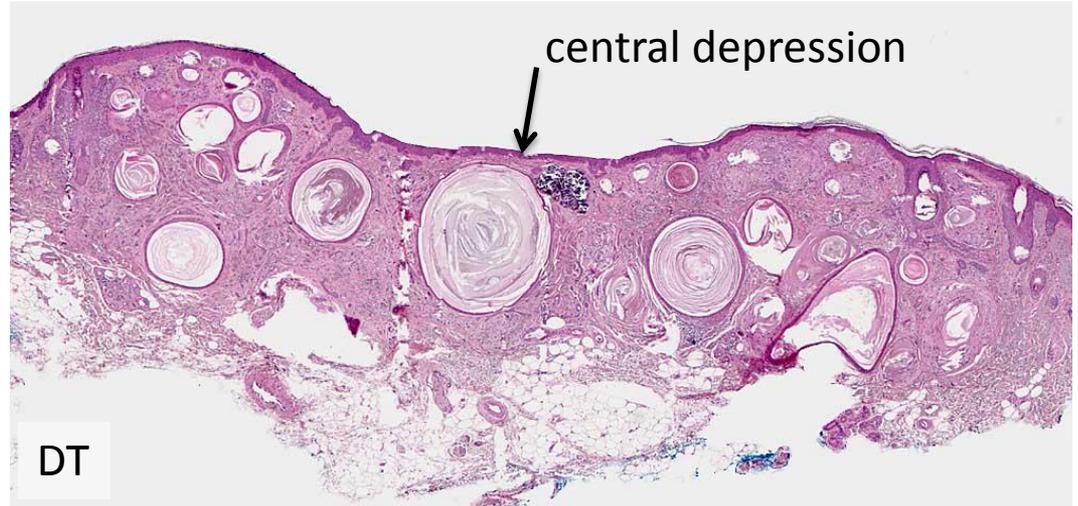
Infiltrative non-sclerodermiform →

Infiltrative sclerodermiform ↓

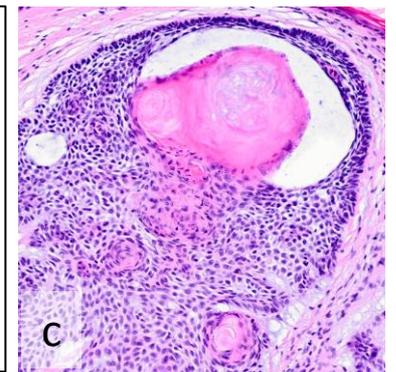
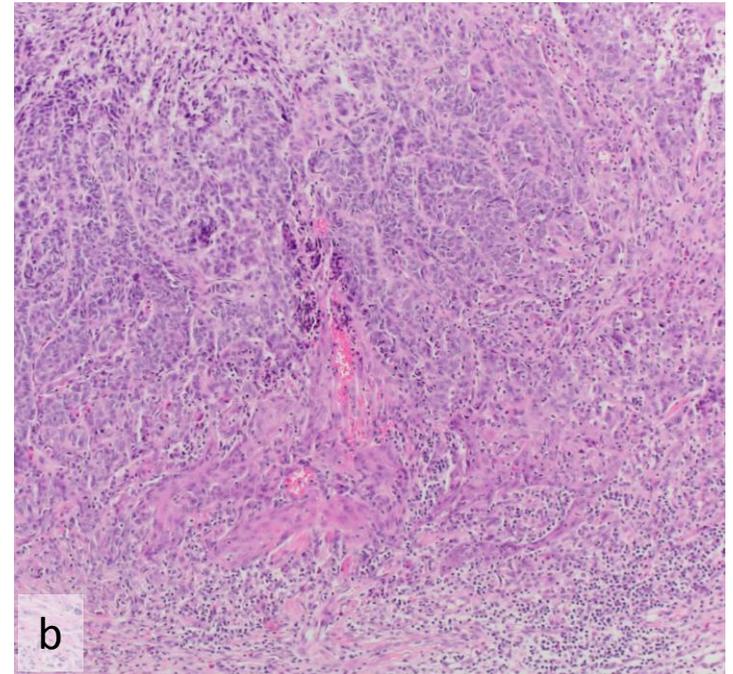
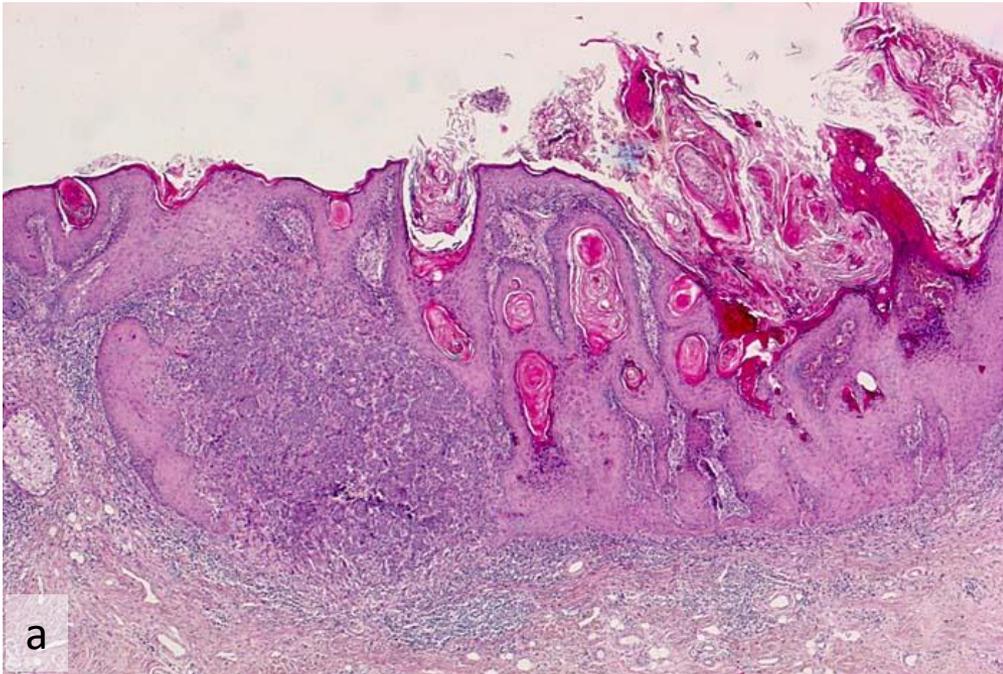


DD: Desmoplastic Trichoepithelioma

Morpheic BCC	DesmoTricho
Ki67>10%	Ki67<10%
bcl-2 diffuse	bcl-2 peripheral
BerEP4 diffuse	BerEP4 focal
No Merkel cells	CK20+ Merkel cells

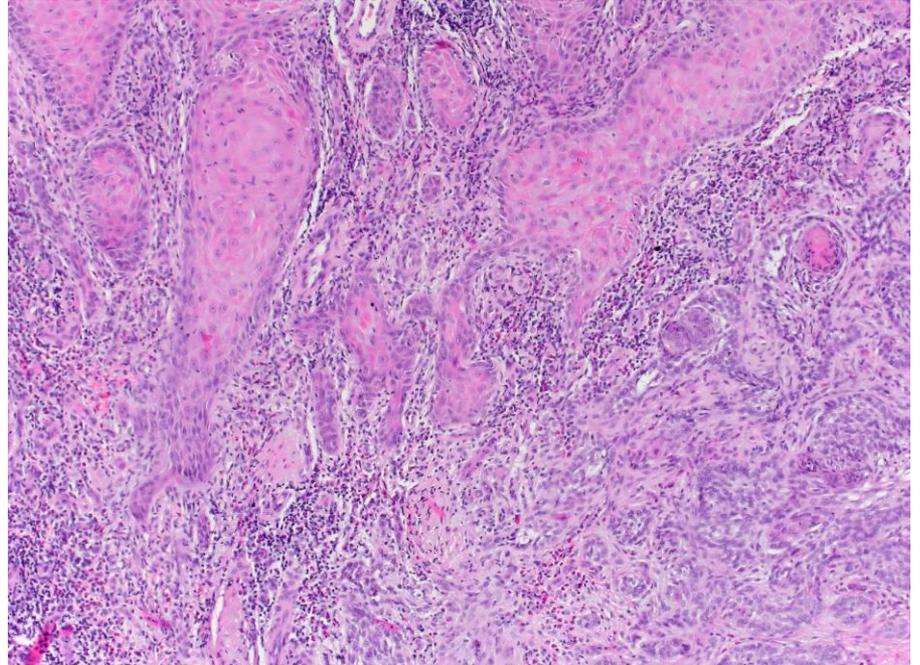
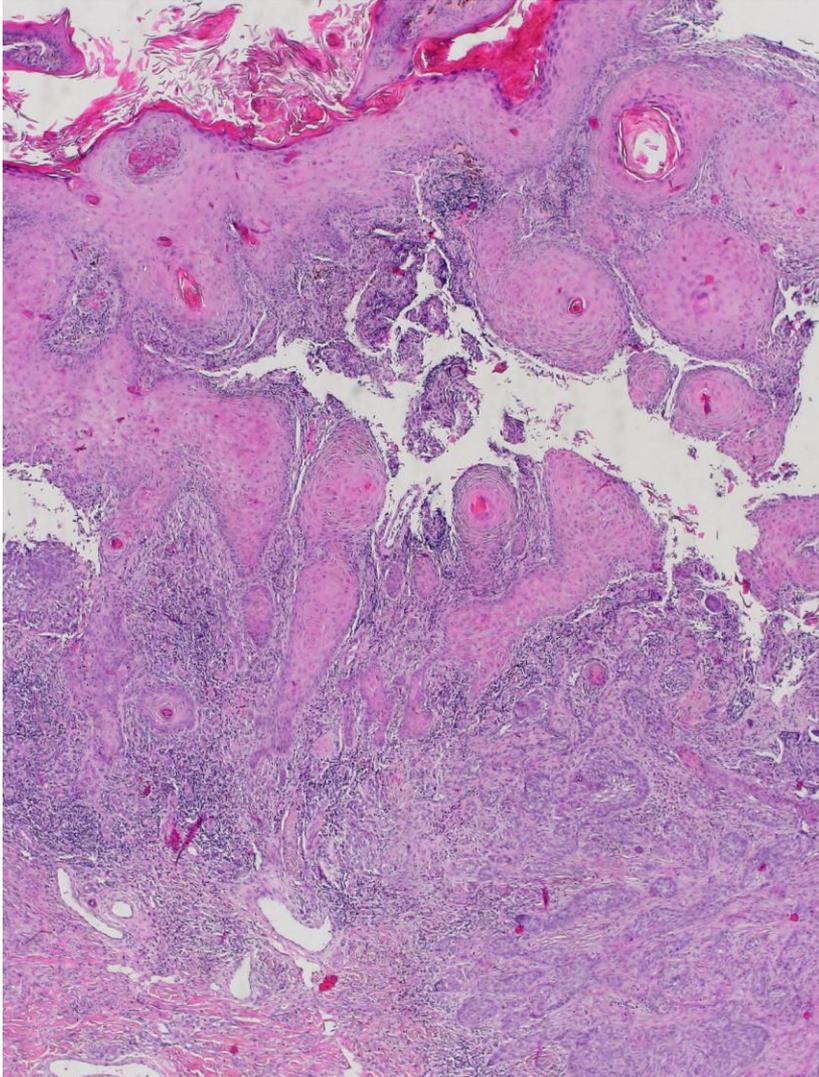


BCC & Squamous Differentiation



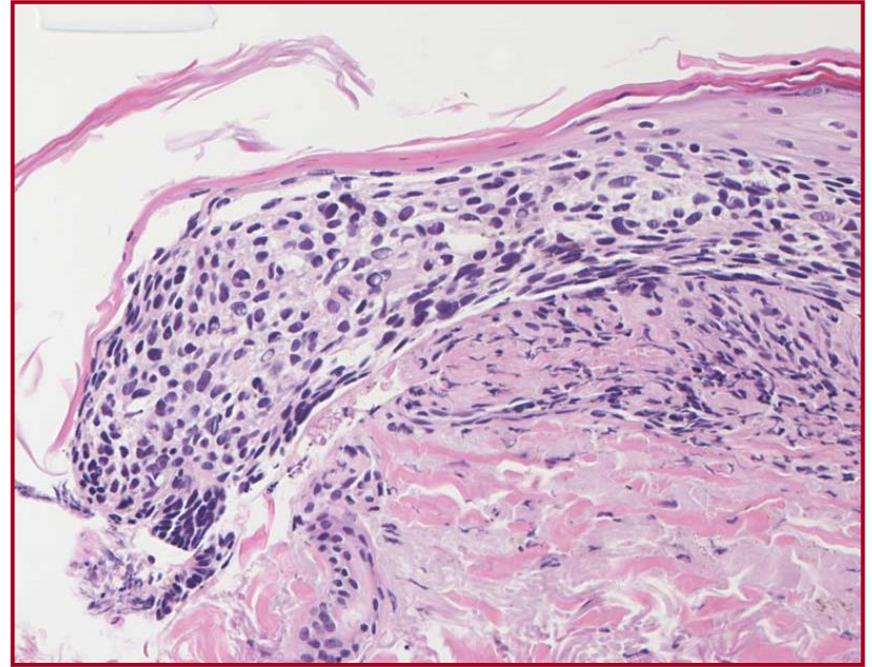
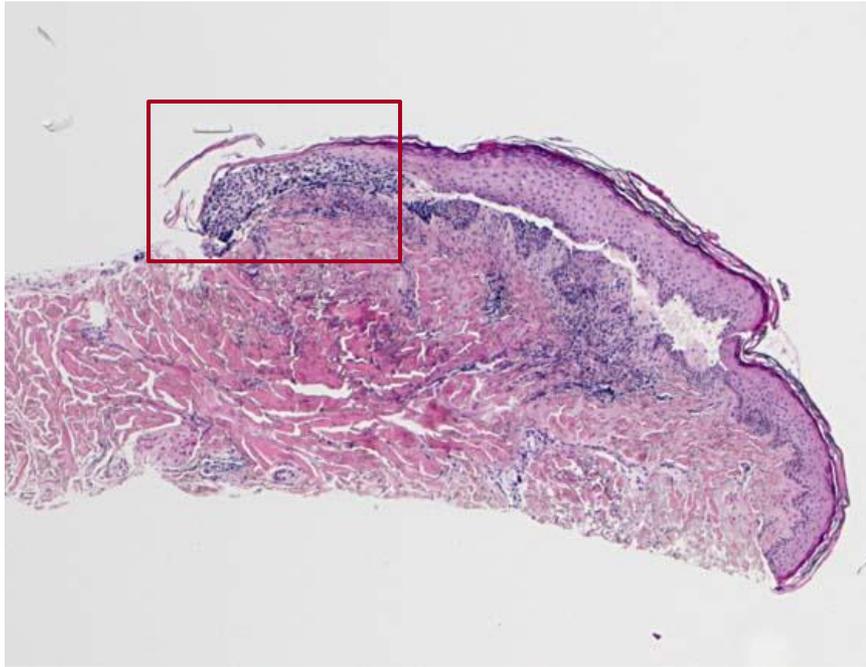
Collision tumors: BCC and SCC as separate tumors (a)
Metatypical BCC (b) and basosquamous BCC
Small foci of keratinization within BCC (c)
SCC with basaloid peripheries vs. BCC with keratotic differentiation
BCC with pseudoepitheliomatous hyperplasia (ff)
Bowenoid actinic keratosis imitating superficial BCC (ff)

Pseudoepitheliomatous Hyperplasia



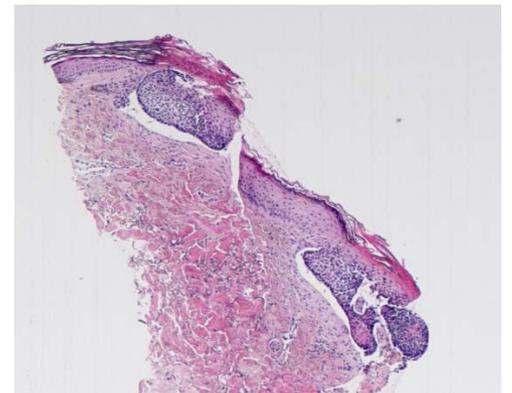
Basal cell carcinoma-associated
paratumoral follicular and
epidermal hyperplasia.
Am J Dermatopathol 2010; 32(4): 348-107.
Abenzoza et al.

Superficial BCC vs. Actinic Keratosis



Actinic keratosis vs. superficial BCC in superficial biopsies:

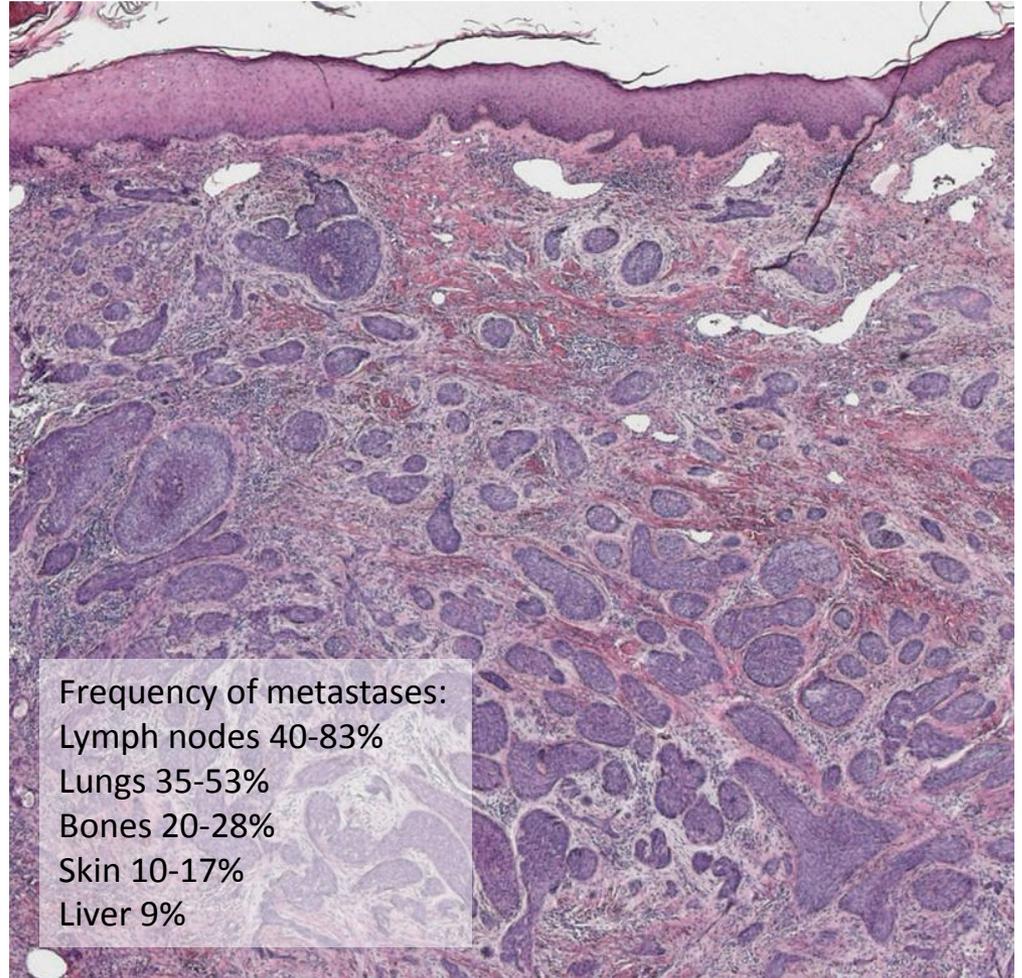
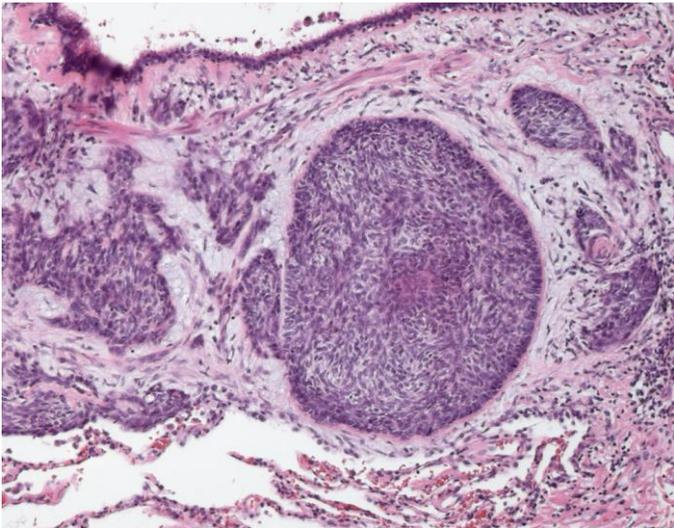
1. Step sections
2. IHC:
Ber-EP4 (BCC +, bowenoid epidermal dysplasia (+))
EMA (SCC +, AK +)



Metastasizing BCC

Risk factors:

Sun exposed area (head&neck)
Large (>10cm²)
Multiple primary BCC
Long-standing lesion
Perineural invasion
Histology: basosquamous,
metatypical, sclerodermiform



Risk Stratification in BCC

Clinical Risk Factors

Size and location

Trunk, extremities ≥ 20 mm

Cheeks, forehead, neck, scalp ≥ 10 mm

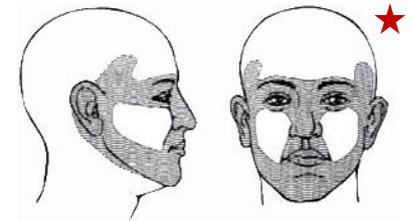
Mask area^{*}, genitalia, hands, feet ≥ 6 mm

Borders poorly defined

Primary vs. recurrent Recurrent

site of prior radiation yes

immunosuppression yes



A single high-risk factor places the patient in a high-risk category

Pathologic Risk Factors

Perineural involvement yes

Histopathologic subtypes micronodular, infiltrative, sclerodermiform

Am J Dermatopathol
2012; 34(7): 737-745

Surgical Margins

Recommendations for Clinical Margins

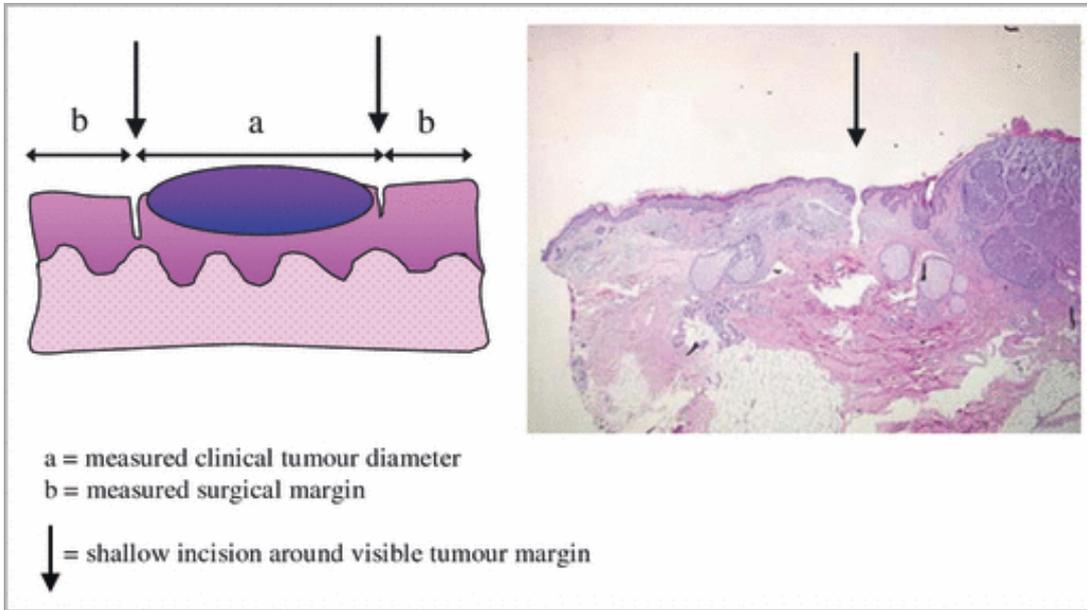
Low risk

4 mm margin of normal appearing skin

High risk

Mohs Surgery (0-11% recurrences)
or resection with complete circumferential peripheral and deep margin assessment

Tissue Shrinkage



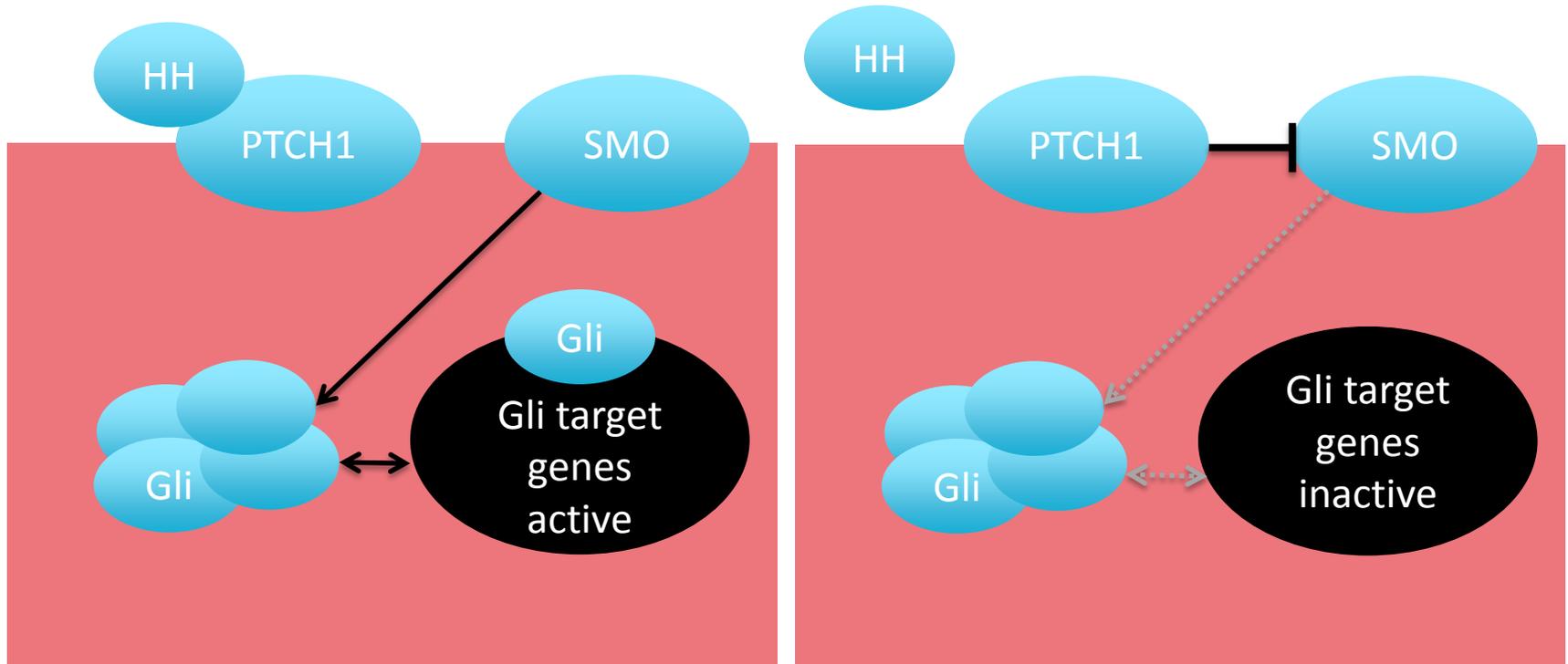
14% shrinkage

a 11% skin with tumor
b 19% normal skin

Effect of tissue shrinkage on histological tumour-free margin after excision of basal cell carcinoma

C. Blasdale et al. British Journal of Dermatology, 2010; 162 (3):607-610

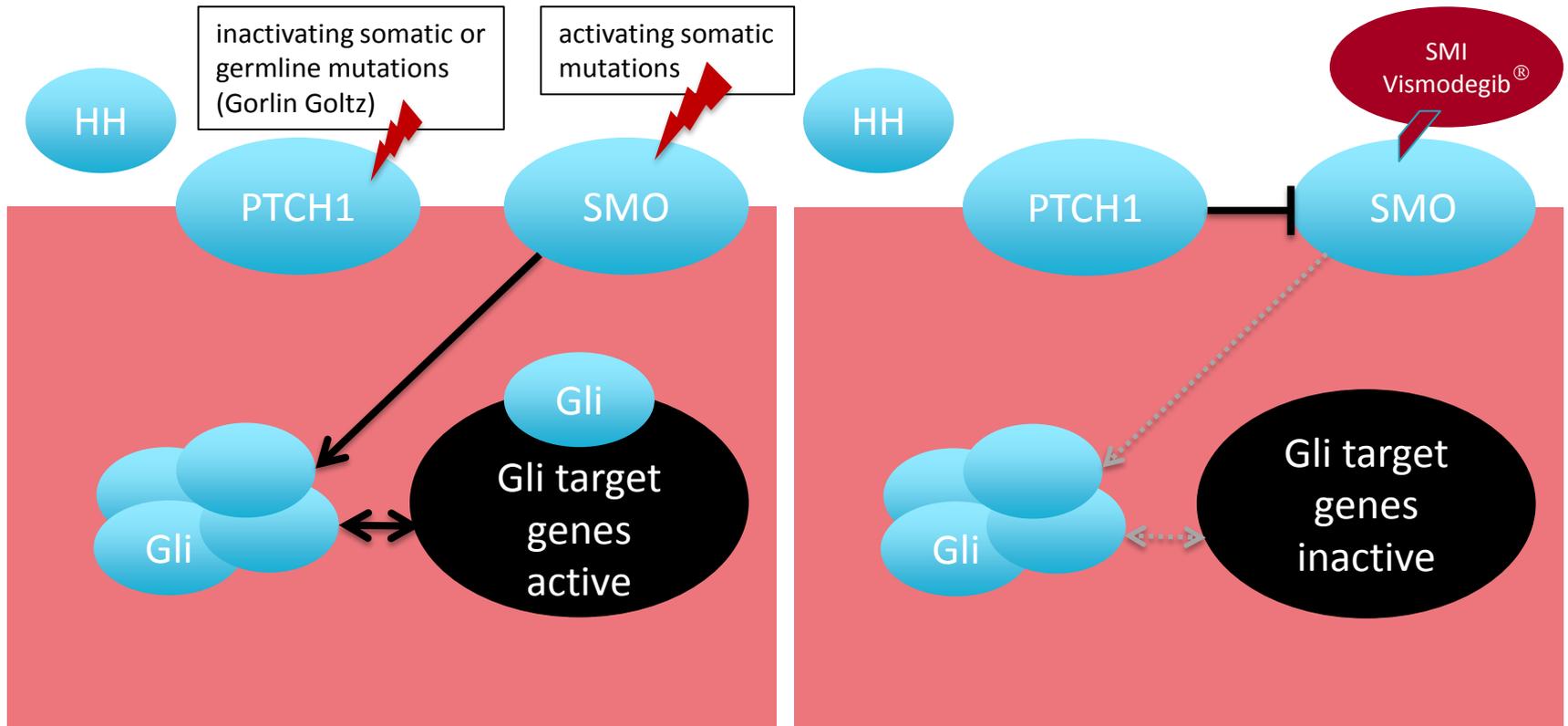
Normal Sonic Hedgehog Pathway



Embryo: active Hedgehog signaling

Normal adult: HH signaling repressed by patched

Sonic Hedgehog Pathway in BCC



BCC: reactivation of HH signaling

targeted therapy: selective inhibition of HH signaling