

### INTRODUCTION

#### Cutaneous Squamous Cell Carcinoma (cSCC)

- Second most common skin cancer (to BCC)
- More aggressive and poorer prognosis
- Progression: actinic keratosis → SCC in situ → SCC
- Separate AJCC staging guidelines specific to cSCC

#### Patient Risk Factors

- UV exposure
- Immunosuppression
- Radiation or carcinogen exposure
- HPV infection
- M>F; more common in fair skin
- Rising incidence

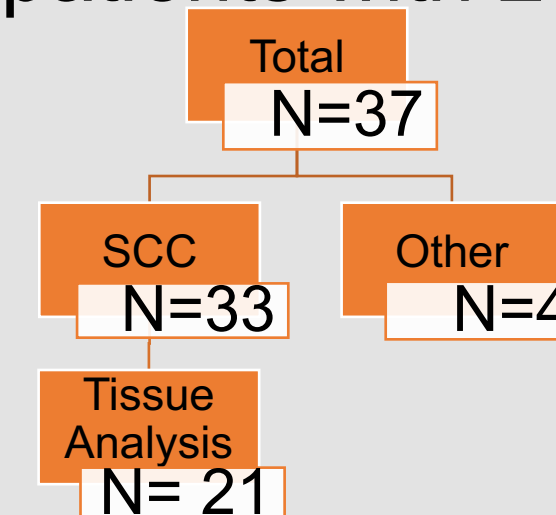


Prognostic factor	Comment
Tumour size	Tumour size (diameter greater than 2 cm) correlates with higher risk of recurrence and metastases
Tumour site	Lesions on the central face, especially around the eyes, nose, lips and ears are at higher risk of recurrence
Definition of clinical margins	Poorly defined lesions are at higher risk of recurrence
Histological subtype	Poorly differentiated confer higher risk of recurrence and metastases
Histological features of aggression	Perineural and/or perivascular involvement confers higher risk of recurrence
Failure of previous treatment	Prior non-melanoma skin cancers Recurrent lesions are at a higher risk of further recurrence and metastases
Immunosuppression and Patient characteristics	Confers increased risk of recurrence and metastases (e.g. recipients of solid-organ transplants); Patient unable to tolerate surgery or radiation due to comorbidities

### PATIENT CHARACTERISTICS

#### Patient Demographics

- 30 individual patients with 33 tumours (3 patients with 2 tumours)
- Average age 78.9 (49-93) years
- 76.5% males



#### Comorbidities

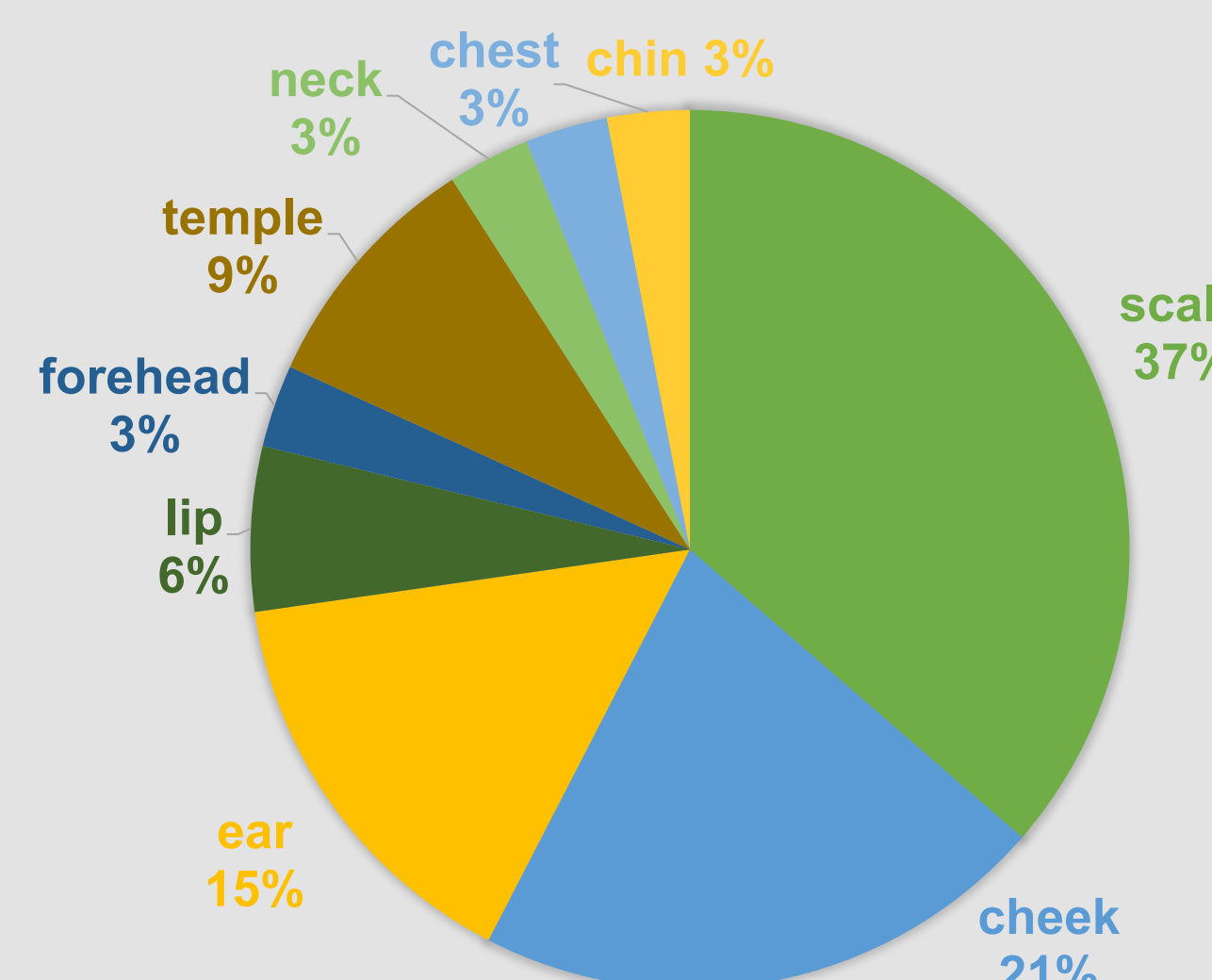
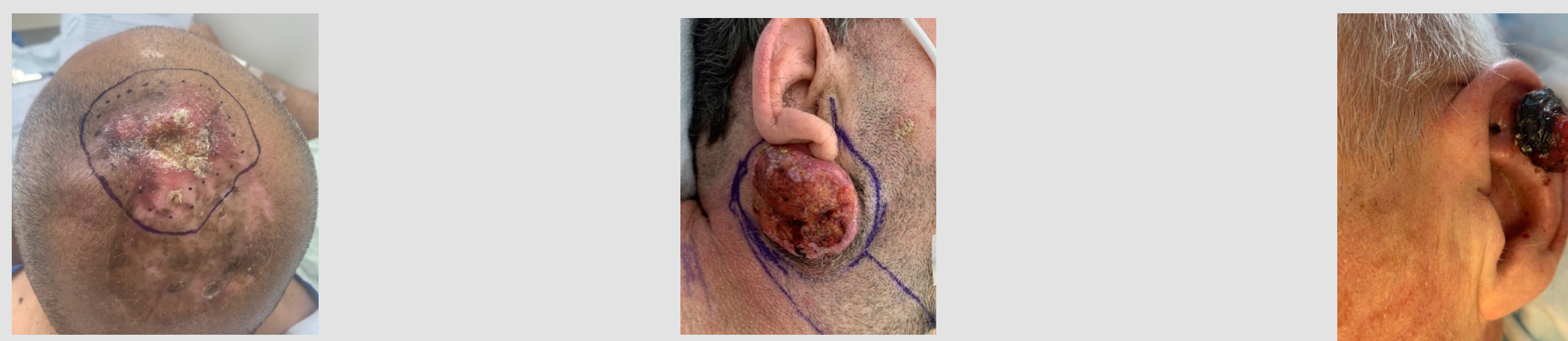
- 76.7% of patients had **prior skin cancers**
- Reasons for immune suppression:
  - Transplant (n=3)
  - Rheumatoid arthritis (n=2)
  - CNS vasculitis (n=1)
  - Crohn's disease (n=1)

Cardiovascular (HTN, dyslipidemia, MI, CAD, heart transplant, AAA, arrhythmia, valvular, CHF, angina)	73.3%
Diabetes	36.7%
MSK (OA, RA)	33.3%
GI (GERD, IBD, CRC, diverticulosis)	30.0%
GU (CKD, transplants, bladder cancer)	20.0%
Respiratory (PE, asthma, COPD, ILD)	16.7%
Previous cancers (prostate, bladder, colon)	16.7%
Neurologic (peripheral neuropathy, stroke, hearing loss, Parkinson's)	13.3%
Ophthalmologic (macular degeneration)	6.7%
Hematologic (polycythemia, anemia)	6.7%
Immunosuppression	23.3%

#### Selected Medications

- 70% of patients on medications for Metabolic Syndrome (anti-hypertensives, statins, blood thinners)
- 30% for diabetes management
- 23.3% on immune suppressants (steroids, mycophenolate, tacrolimus, methotrexate, biologics)
- 20% for pain control

#### Anatomic Locations

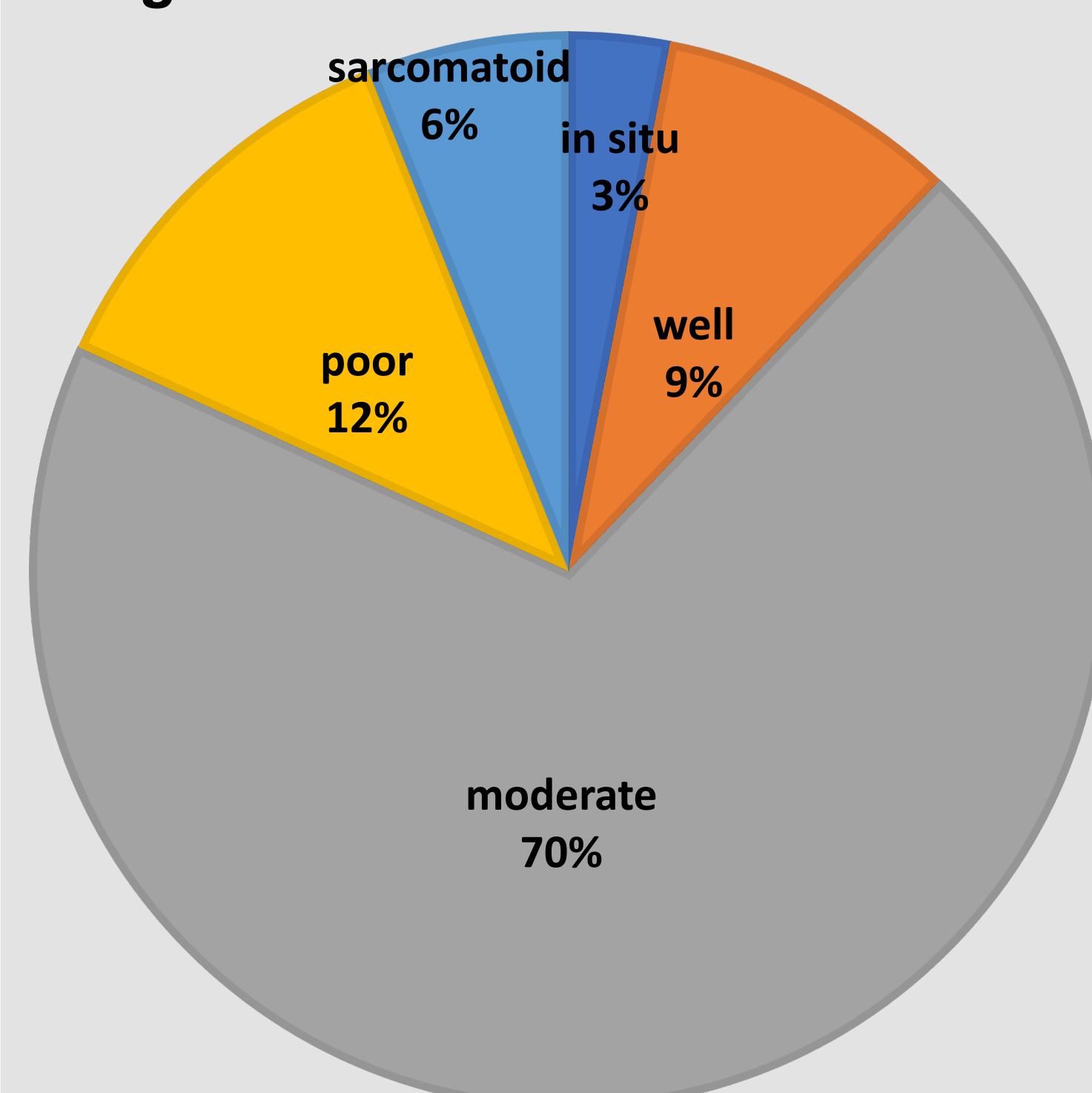


### TUMOUR CHARACTERISTICS

#### Size and Differentiation

- Average size = 3.1 cm largest dimension (0.6 – 8.1 cm)

#### Degree of Differentiation



AJCC Tumour Stage	Percentage
TisN0M0	3.0%
T1N0M0	12.1%
T2N0M0	18.2%
T3N0M0	57.6%
T3N0M1	6.1%
T3N3aM0	3.0%

### PATIENT OUTCOMES

Adjuvant radiation	18.2%
Immunotherapy	12.1%
Local recurrence	15.2%
Regional recurrence	12.1%
Metastasis	12.1%
Mortality*	3.0%

Degree of Invasion	Percentage
Lymphovascular Invasion	13.3%
Perineural Invasion	23.3%
Deep Invasion	50.0%

\*patient died of urosepsis, not cSCC

### APPLICATIONS OF DATABASE: GAPS IN CARE

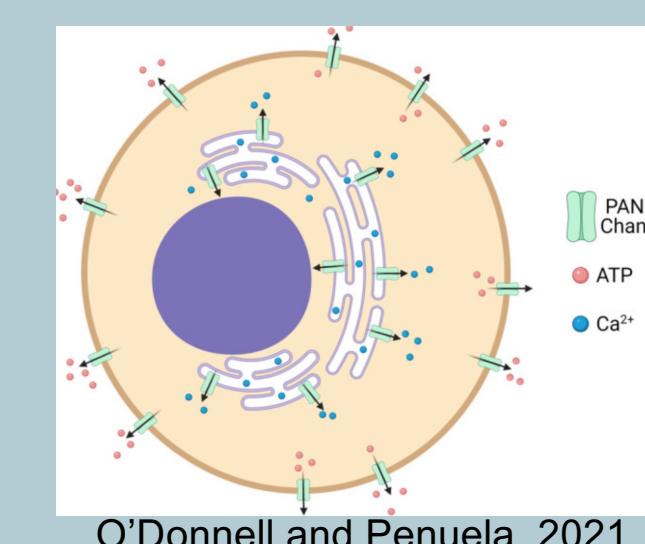
**Objectives:** Identify outcomes, treatment options, and gaps in care among patients with high risk cSCC presenting to regional cancer centers through the development of a national database of cutaneous SCC patients.

- Despite rising incidence, there are few comprehensive databases cataloguing detailed pathology results or treatment outcomes.
- Studying gaps in care high-risk cSCC is timely
  - many jurisdictions restructuring funding towards Quality-Based Programs
  - Emergence of immunotherapy is impacting therapy choices
- Address gaps in patient care in terms of presentation, time to biopsy, imaging & decision to treat
- Understand current management algorithms & optimal timing of treatment with Canadian perspective.

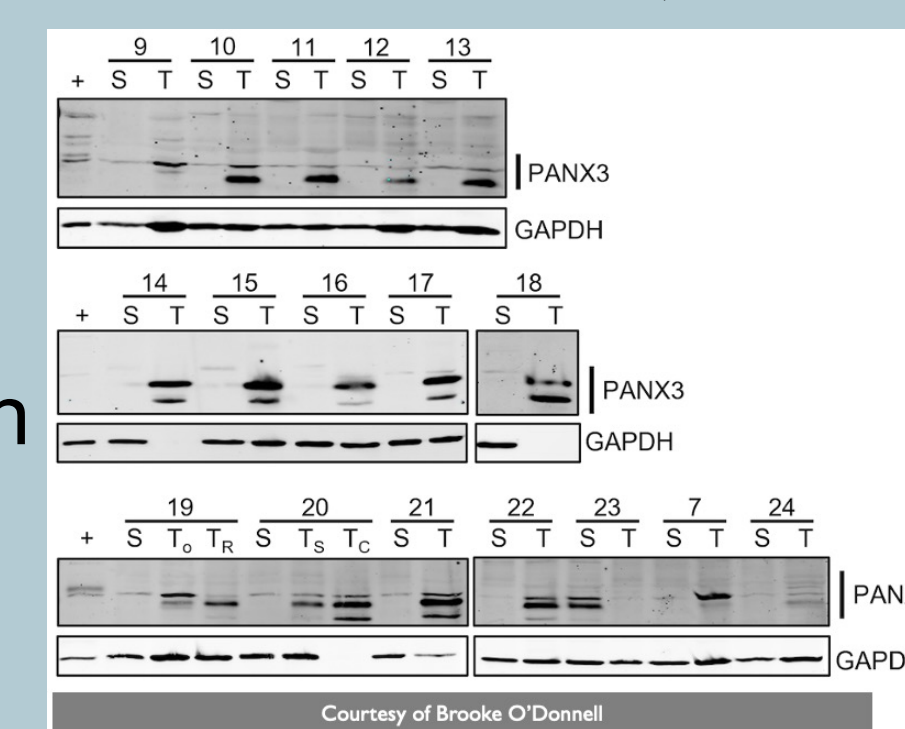
### APPLICATIONS OF DATABASE: PANNEXIN3

Correlation of epidemiological data to bench research

- Single membrane channel-forming glycoprotein for signaling molecules (ATP and Ca<sup>2+</sup>)
- Predominant in skin, cartilage and bone
- Regulates balance of keratinocyte proliferation and differentiation
- Implicated in non-melanoma skin cancer; precise role unclear
- Preliminary data show PANX3 increased in cSCC



O'Donnell and Penuela, 2021



Courtesy of Brooke O'Donnell

### PRELIMINARY CONCLUSIONS

- Consistent with known SCC epidemiological data, patients are predominantly males over 75 years old
- Average tumour size is 3.1 cm
- Most commonly stage T3N0M0 (stage 3) at presentation
  - Want to understand biology of intermediate stage tumours better as they are ideal target for treatment
- 50% have deep invasion
- 15.2% local recurrence rate, 12.1% rate of nodal recurrence
- Tumours with more aggressive features have worse outcomes

### LIMITATIONS AND FUTURE DIRECTIONS

#### Limitations

- Early prospective data (avg length of follow-up = 1.2 yrs)
- Collection bias of tissue samples
  - Tissue collected from OR so tumours are intermediate size and stage
  - Too small = insufficient tissue
  - Too large = bloody, necrotic (some samples degraded)

#### Future Directions

- Continue to follow cohort over time as data matures
- Follow recurrence, metastasis, mortality
- Collect gaps in care data
- Grow national database with Sunnybrook & LHSC
- Compare late (recurrent, nodal) vs intermediate stage disease

#### PANNEXIN3:

- Assess mRNA expression levels
- Correlate clinical data to expression data
- Understanding of molecular basis could identify modifiable targets and prognostic factors

### AIMS

- 1 Develop a clinical database of patients presenting with advanced cutaneous SCCs
- 2 Characterize the role of pannexin-3 channels in human cutaneous SCCs
- 3 Correlate clinical patients characteristics and features of tumours with pannexin-3 expression

### METHODS

- Prospectively (April 2021 onwards) collected data from patients who underwent excision for advanced cutaneous SCC of the head and neck region at LHSC
- Demographic data, patient factors, tumor factors and outcomes collected from patient charts

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