

Nathalie Heynickx^{1,2}, Ken Herrmann^{3,4}, Koen Vermeulen¹, Sarah Baatout^{1,2}, An Aerts¹

¹: Belgian Nuclear Research Centre, SCK CEN, Mol, Belgium

²: Department of Molecular Biotechnology, Ghent University, Ghent, Belgium

³: Department of Molecular and Medical Pharmacology, David Geffen School of Medicine UCLA, Los Angeles, CA, United States of America

⁴: Department of Nuclear Medicine, Medical faculty, University Hospital Essen, Essen, Germany

E-mail: nathalie.heynickx@sckcen.be

Goal

Summarize the current literature available on salivary gland toxicity after PSMA-targeted radionuclide therapy.

Methods

Literature search on:

- Salivary gland toxicity after ERBRT
- Salivary gland toxicity after PSMA-TRT
- Preventive and/or treatment strategies of salivary gland toxicity

Introduction

- Prostate cancer remains a significant health burden
- PSMA-targeted radionuclide therapy is emerging as a new treatment modality
- Uptake of PSMA-targeting compounds in healthy tissues results in healthy organ toxicity

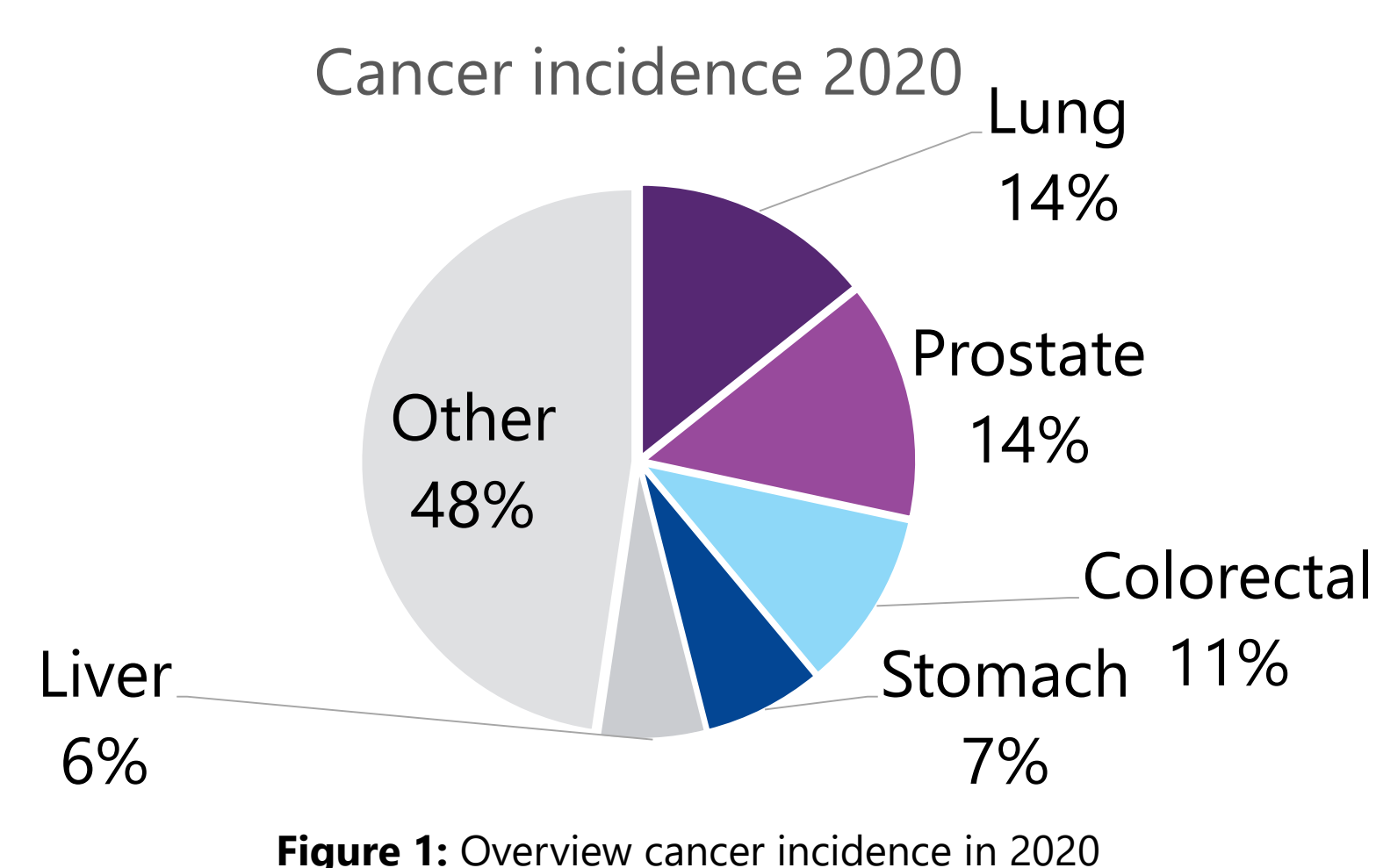
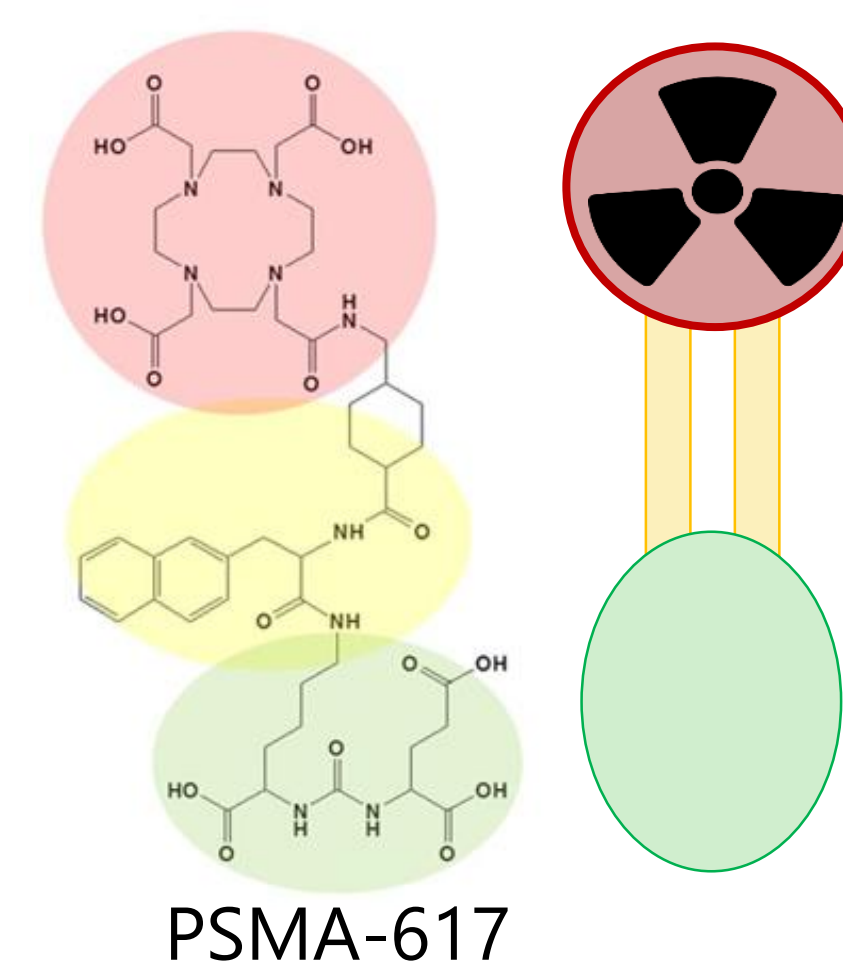


Figure 1: Overview cancer incidence in 2020



PSMA-617

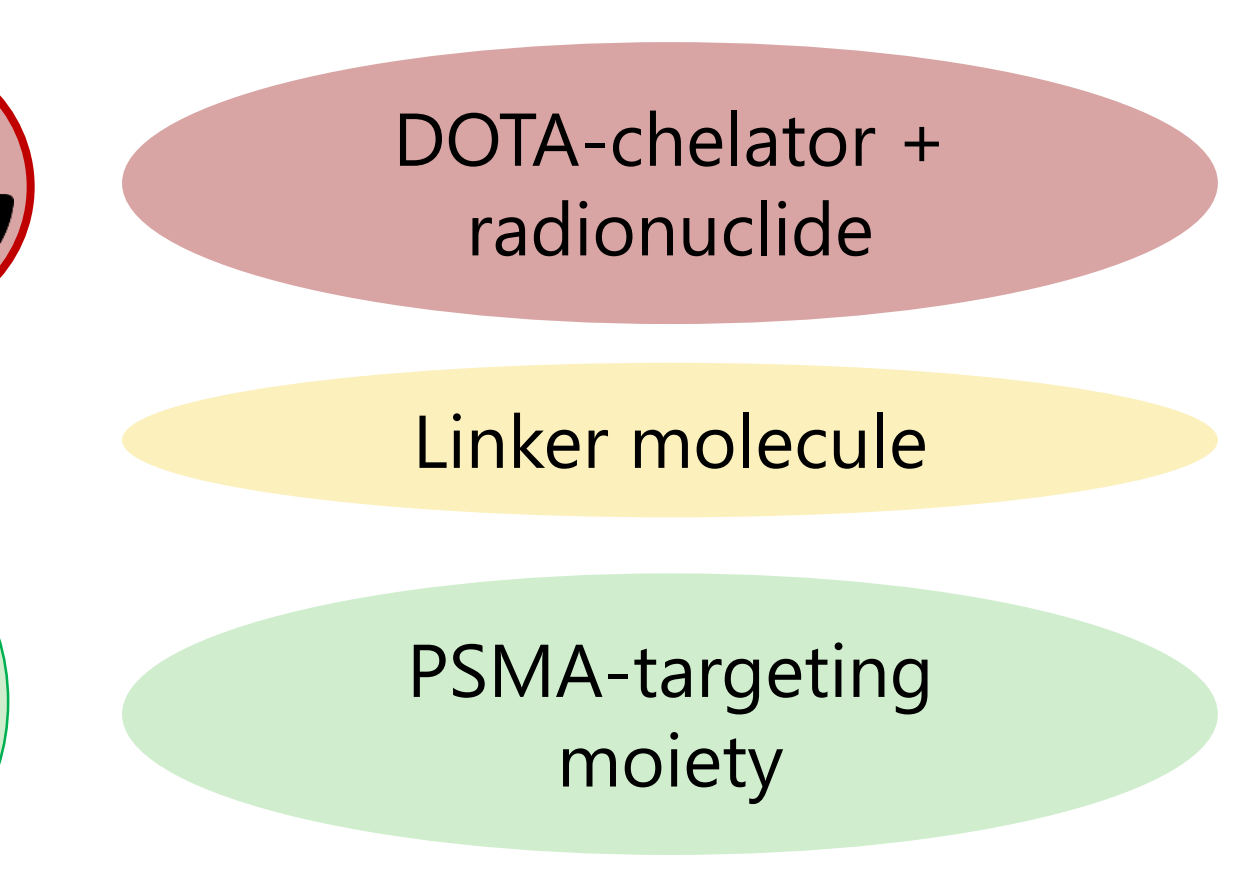


Figure 2: Overview of the compound PSMA-617 and its schematic representation

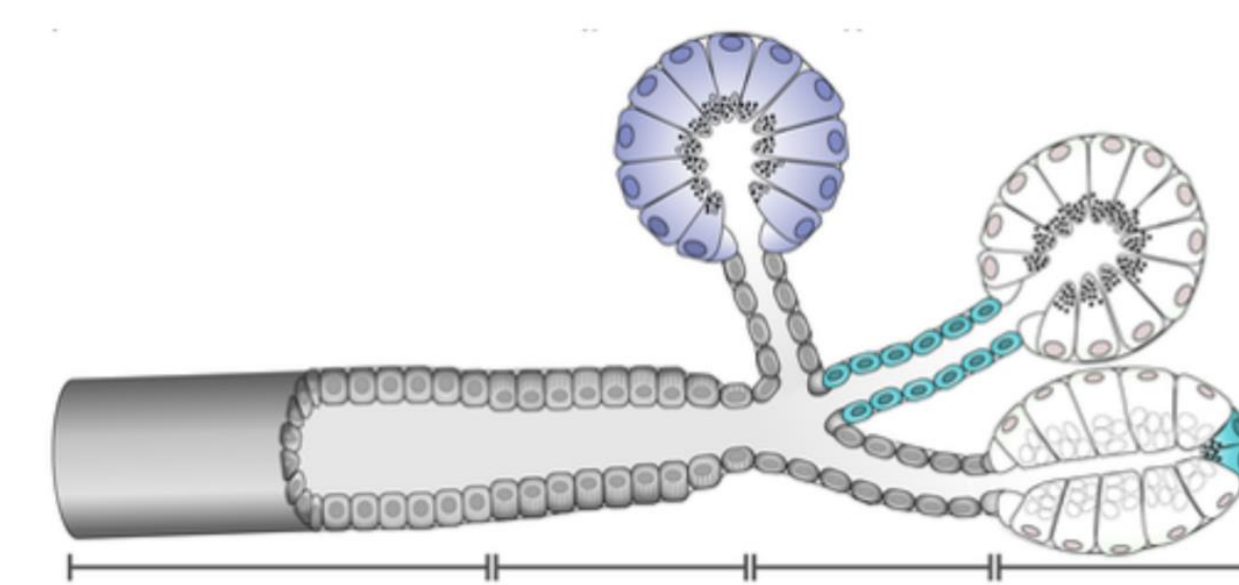
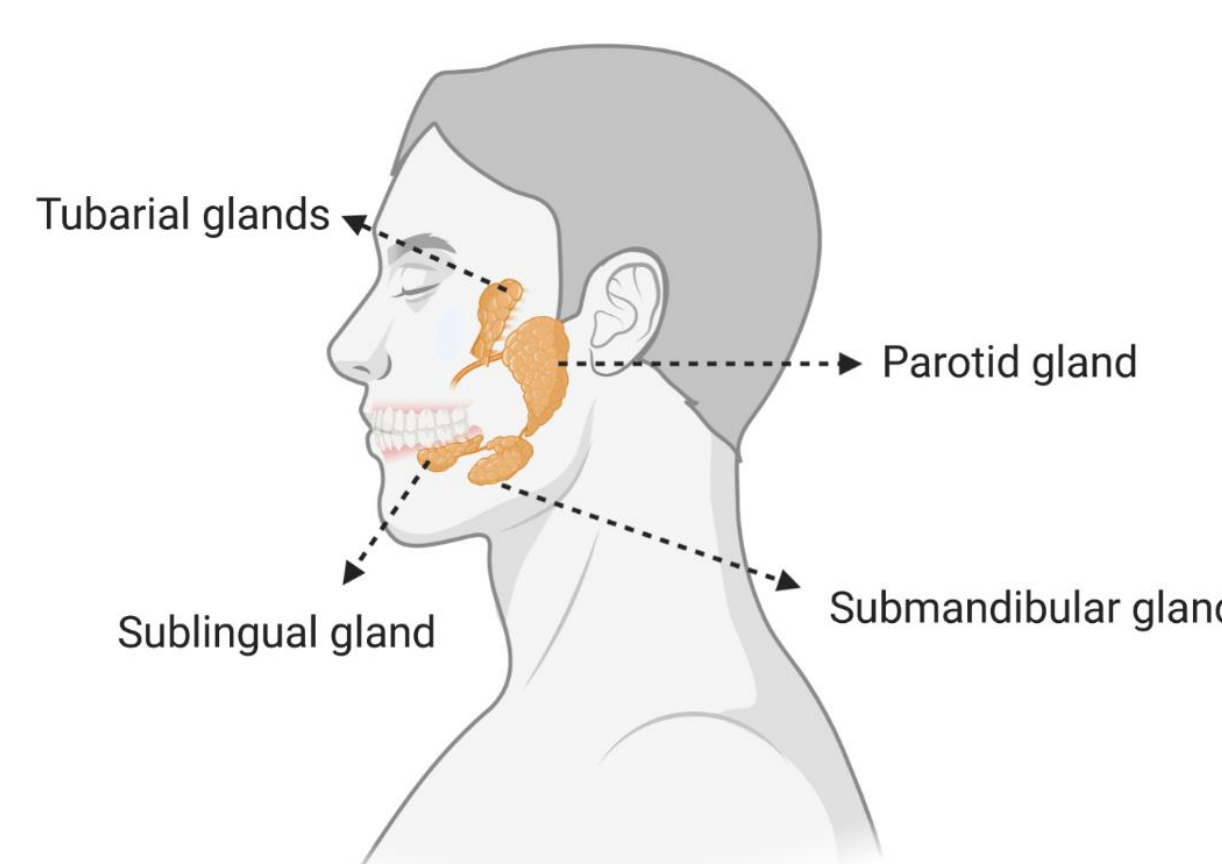


Figure 3: Overview of the human salivary glands and their histological structure

Problem

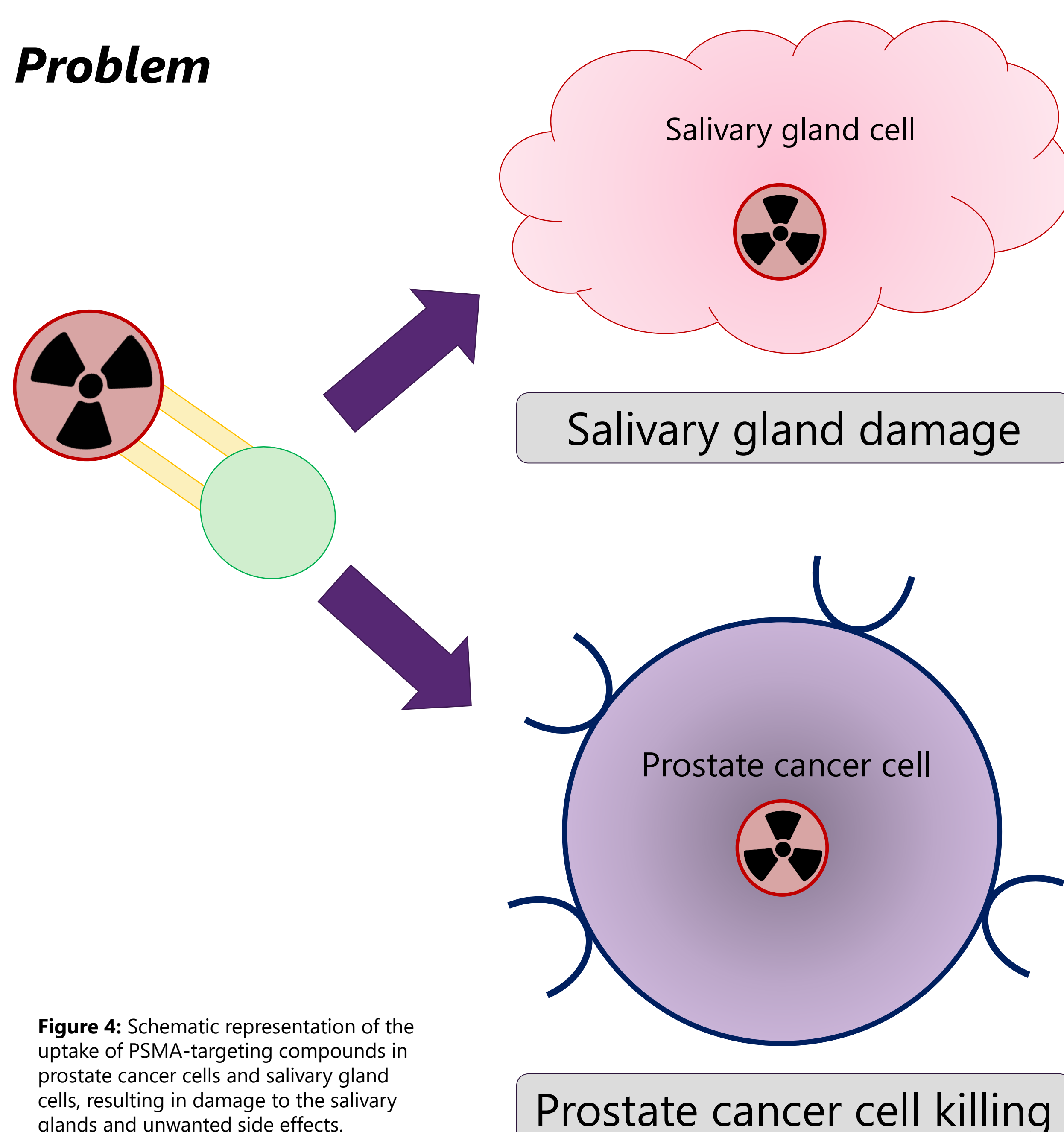


Figure 4: Schematic representation of the uptake of PSMA-targeting compounds in prostate cancer cells and salivary gland cells, resulting in damage to the salivary glands and unwanted side effects.

Table 1: Overview of the 4 different phases of salivary gland damage

Phase	Time after radiation exposure	Main characteristics
1	0 to 10 days	• No loss of salivary gland cells • Severely impaired water excretion
2	10 to 60 days	• Disappearance of acinar cells • Disappearance of amylase secretion • No net compensation of lost cells
3	60 to 120 days	• No major changes in salivary gland cells and salivary flow rate
4	120 to 140 days	• Shortage of functional acinar cells • Loss of parenchymal cells • Generation of new dysfunctional acinar cells • Further deterioration of amylase secretion and salivary flow rate

Preventive or treatment strategies

- Most knowledge on salivary gland damage comes from research after external beam radiotherapy
- There is a lack of knowledge on uptake and damage mechanisms of PSMA-targeting compounds
- Research on potential preventive and/or treatment compounds for salivary gland toxicity showed no or only limited efficacy

Conclusion

- Summary on current knowledge of salivary gland damage after EBRT, reflecting towards PSMA-TRT of which researchers in the field can benefit
- Highlights the need for further understanding of salivary gland damage after PSMA-TRT to design more effective preventive and/or treatment strategies for salivary gland damage

