# Late toxicities after chemoradiotherapy for anal cancer

# Background

- Late toxicities are clearly underinvestigated in the literature but impact quality of life (QoL)
- „A majority [...] considered bowel and bladder incontinence [...] as health states the same or worse than death“ (Rubin et al. JAMA Intern. Med. 2016)
- Toxicities after CRT: Fecal incontinence, urgency, anal stenosis, ....

# Fecal incontinence

- Only few studies have used **specific assessment tools** (anorectal manometry, PROMs/QoL, St. Marks Incontinence score)
- Rate of (partial) fecal incontinence in these studies: **38 – 44%**
- Rate of colostomies due to sphincter dysfunction: **0.5 – 10.9%**

Bin Pan et al. Acta Oncologica 2018 https://doi.org/10.1080/0284186X.2018.1503713

# Radiation proctitis

- Not mentioned in **RTOG/EORTC** or **LENT-SOMA** criteria
- CTCAE criteria of proctitis overlap with other late toxicities (e.g. G3 -> fecal incontinence)
- Incidence of proctitis after CRT: **0 – 40%**

Bin Pan et al. Acta Oncologica 2018 https://doi.org/10.1080/0284186X.2018.1503713

# Stenosis/Fibrosis/Fistulae

- Anal stenosis occurs in 1-8.5% (older series)
- Fistulae (recto-vaginal, recto-vesical, anal, rectal): 1 – 22.2%
- **ACCORD 03 RT dose-escalation trial:** 3% of patients needed abdomino-perineal resection or colostomy for severe gastrointestinal toxicities (fistulae, necrosis, ulceration, pain, bleeding)→ RT doses above 60 Gy can be critical !

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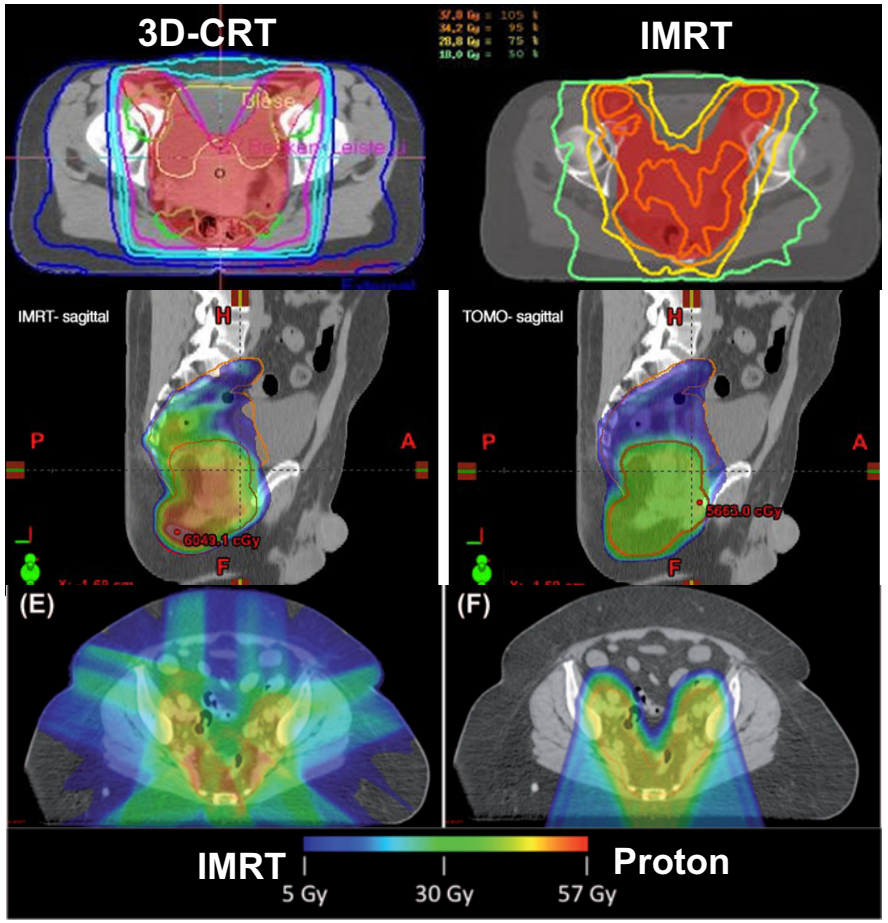
# Modern RT methods to reduce toxicity

## Optimization of external beam

- IMRT (vs 3D-CRT)
- Rotational methods: VMAT, Tomotherapy
- Sequential and simultanous boosting
- IGRT and plan adaptation; protons

## Better sparring of organs at risk

- Bowel and bladder
- Genitalia
- Skin
- Bone marrow*




*Milano et al, IJROBP 2005*
*Joseph et al, 2010 Radiother Oncol 2010*
**Andrew et al, IJROBP 2016*

*Menkarios et al, Rad Oncol 2007*
*Ojerholm et al, Acta Oncol 2015*
**Carmona et al IJROBP 2014*

*Stieler et al, Rad Oncol 2009*
**Robinson et al, Radiother Oncol 2015*
**Rose et al, IJROBP 2016*

# IMRT reduces toxicity compared to 3D-CRT

| Trial | Patients (n) | Modality | ≥G3 skin tox (%) | ≥G3 GI tox (%) | LC (%) |
|---|---|---|---|---|---|
| **Saarilathi 2008** | 39 | 3D-CRT | 32 | 12 | 92 |
| | 20 | IMRT | 16 | 0 | 85 |
| **Bazan 2011** | 17 | 3D-CRT | 41 | 29 | 57 |
| | 29 | IMRT | 21 | 7 | 92 |
| **Dewas 2012** | 27 | 3D-CRT | 33 | 4 | 77 |
| | 24 | IMRT | 37 | 4 | 63 |
| **Chuong 2013** | 37 | 3D-CRT | 65 | 30 | 92 |
| | 52 | IMRT | 11 | 10 | 91 |
| **Kachnic 2013*** | 325 | 3D-CRT | 49 | 36 | 78 |
| | 52 | IMRT | 23 | 21 | 87 |

*Comparison of RTOG 9811 vs RTOG 0529 trial data

# Conclusion

- Late toxicities are not uncommon and vary in frequency in patients with anal cancer
- Recently developed EORTC QLQ-ANL27 questionnaire will help to better understand the impact of these late toxicities on the QoL
- IMRT/VMAT leads to clinically meaningful reduction in acute toxicity; more late toxicity data after IMRT/VMAT in patients with anal cancer are needed
- The ongoing PLATO trials (ACT3-5) will further elucidate the impact of RT-dose escalation/de-escalation on late toxicity after CRT