Late effects of treatment, including Lymphedema

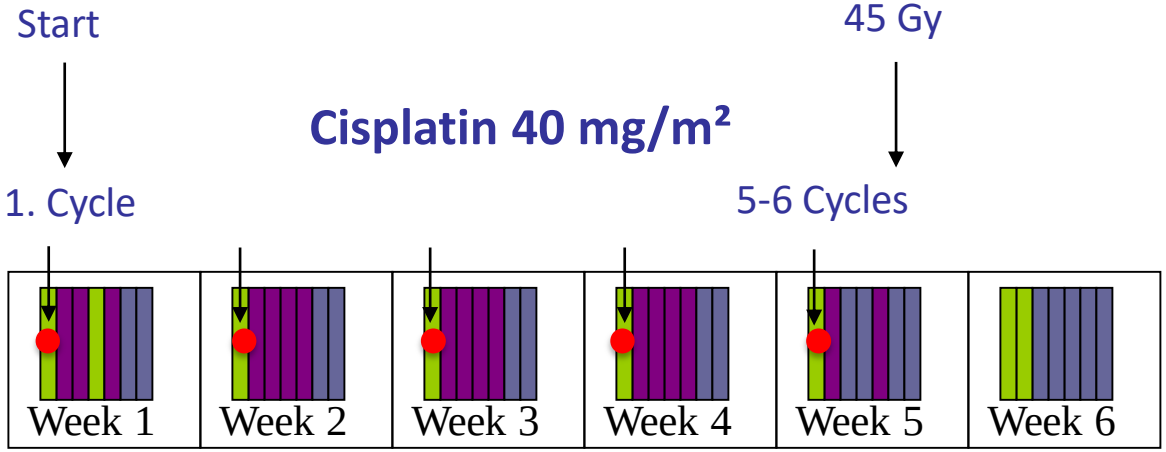
Radiotherapy

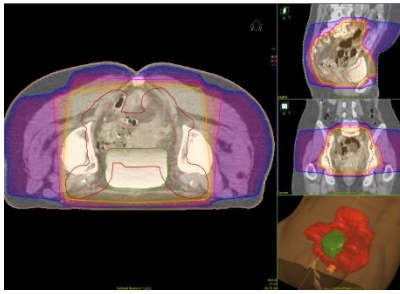
Alina Sturdza, MD, FRCPC

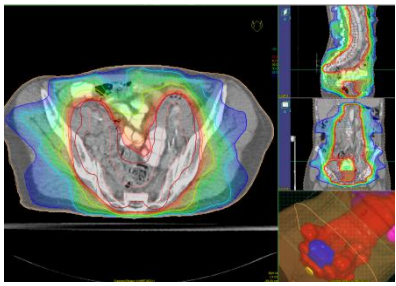
Medical University of Vienna, Austria

Primary radiochemotherapy in cervical cancer

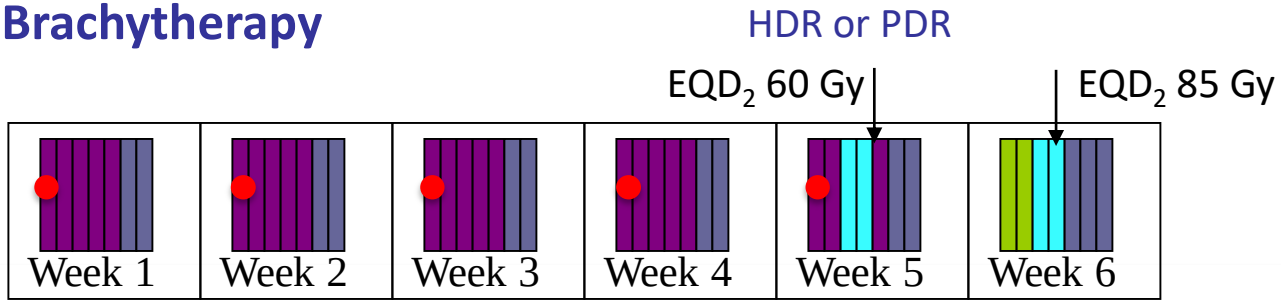
External beam radiotherapy and concurrent chemotherapy

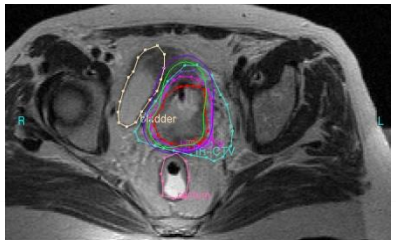






Brachytherapy

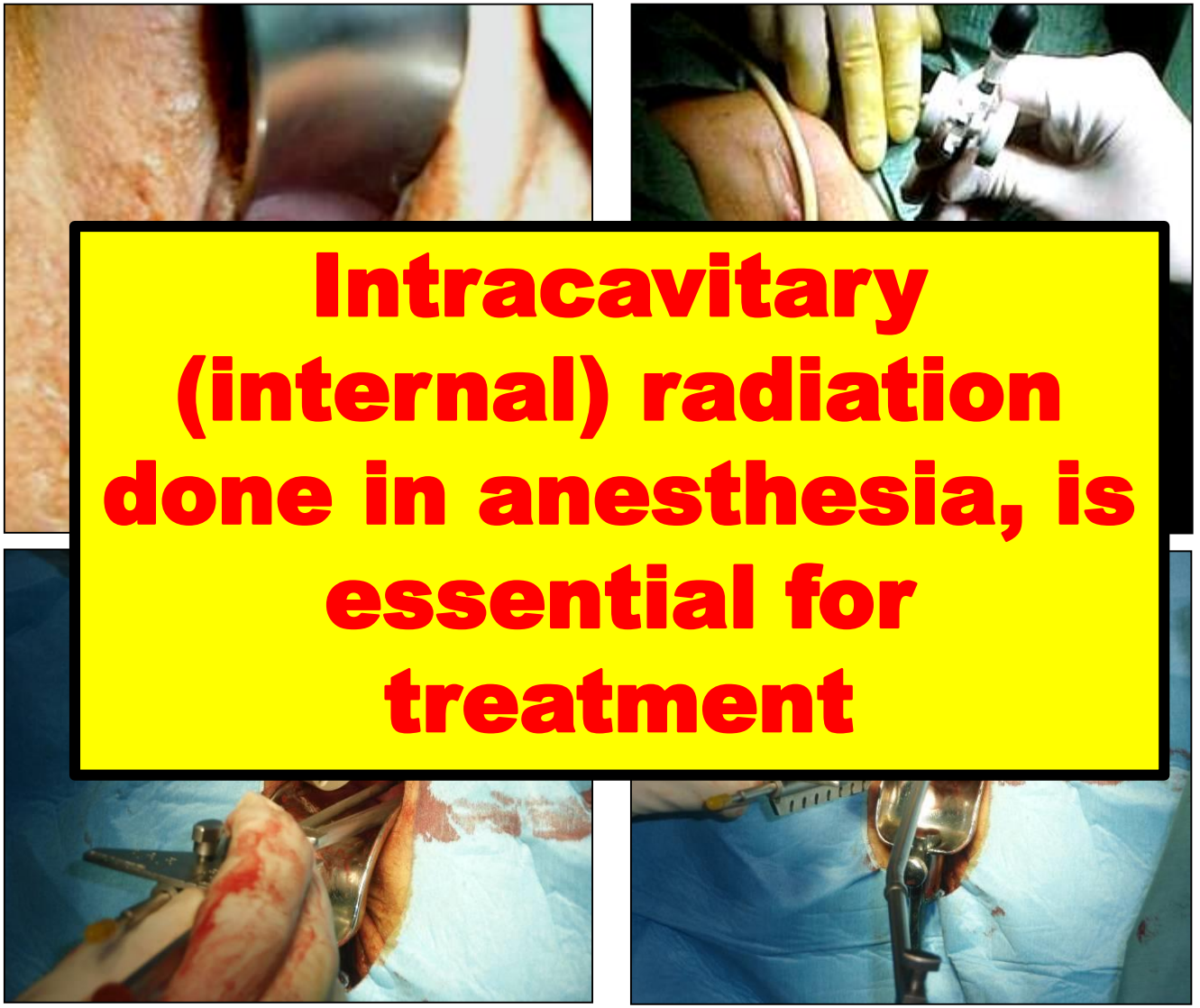




5-7 weeks of treatment with external therapy, chemotherapy and intracavitary (internal) radiation

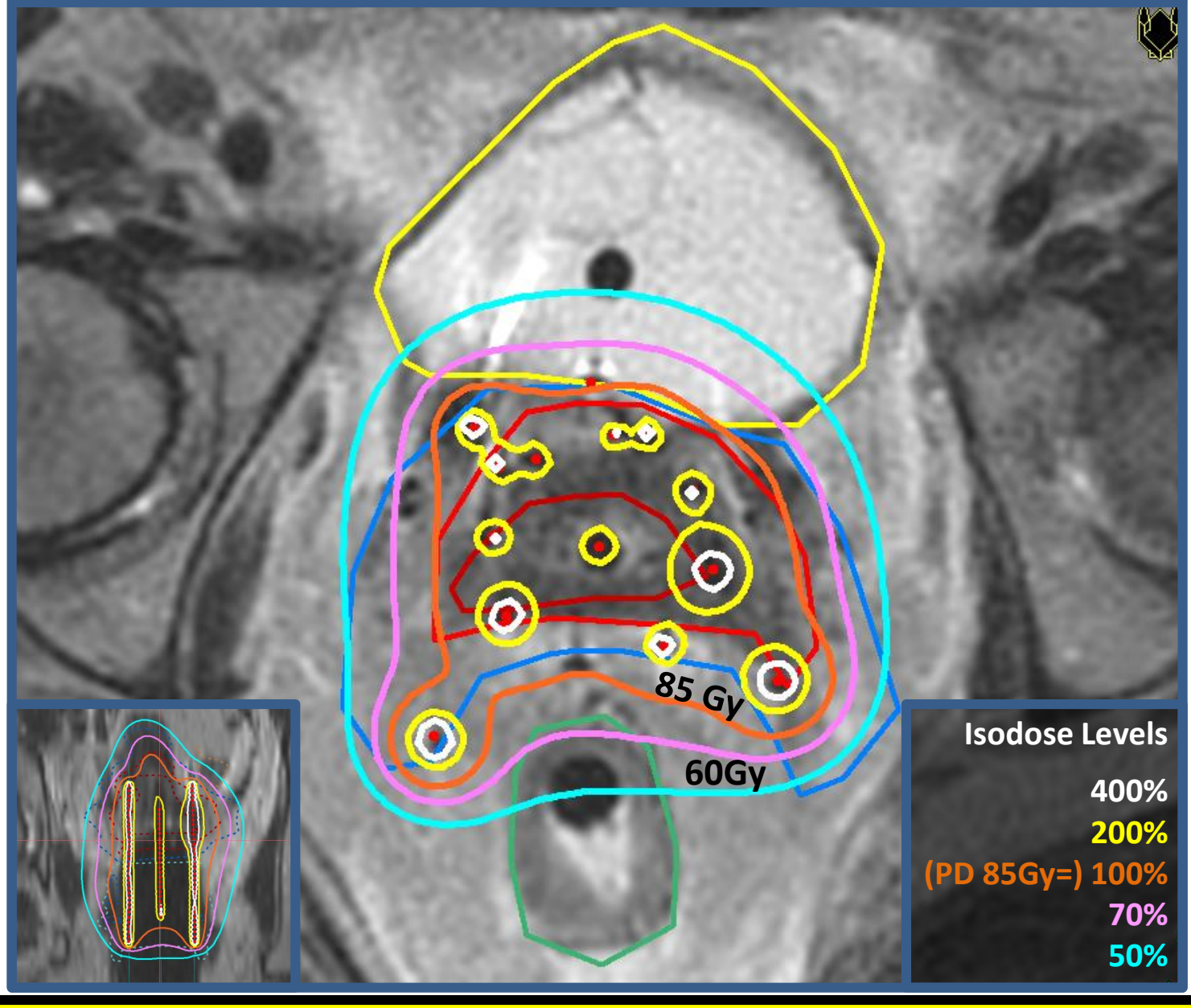
Modern Intracavitary Techniques

Applicator insertion



Intracavitary (internal) radiation done in anesthesia, is essential for treatment

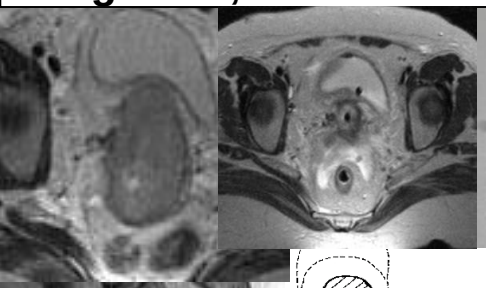
MRI guided Brachytherapy in a FIGO stage IV A cervical cancer patient



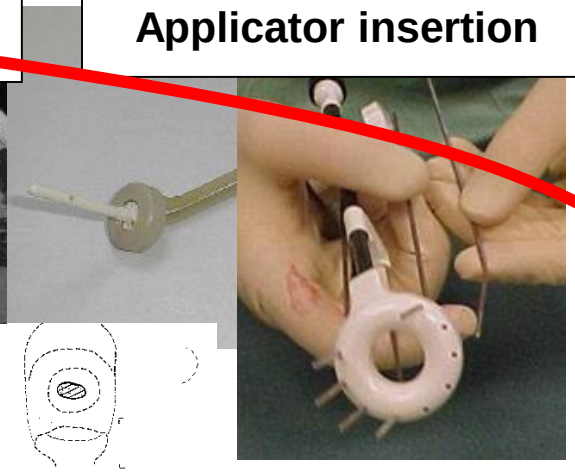
Modern radiation techniques improve normal organ sparing and decrease side effects

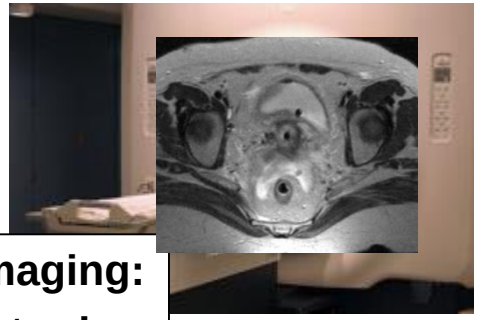
Image-guided adaptive Brachytherapy

Repetitive Imaging diagnosis, EBRT/CHT

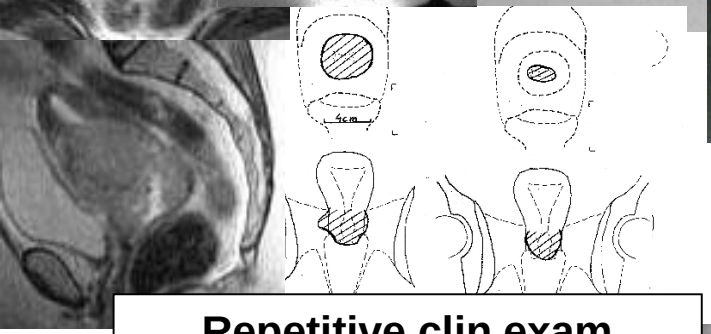


Applicator insertion



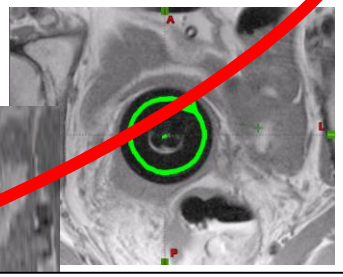


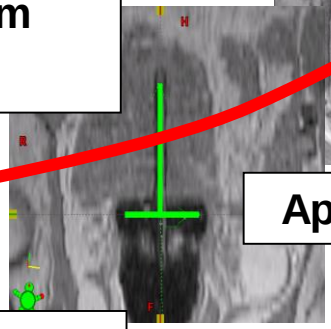
3D/4D imaging: applicator in place



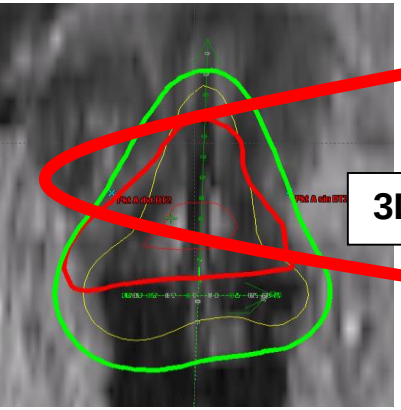
Contouring

Repetitive clin exam +3D/4D drawing

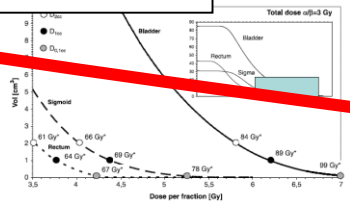




Applicator Reconstruction

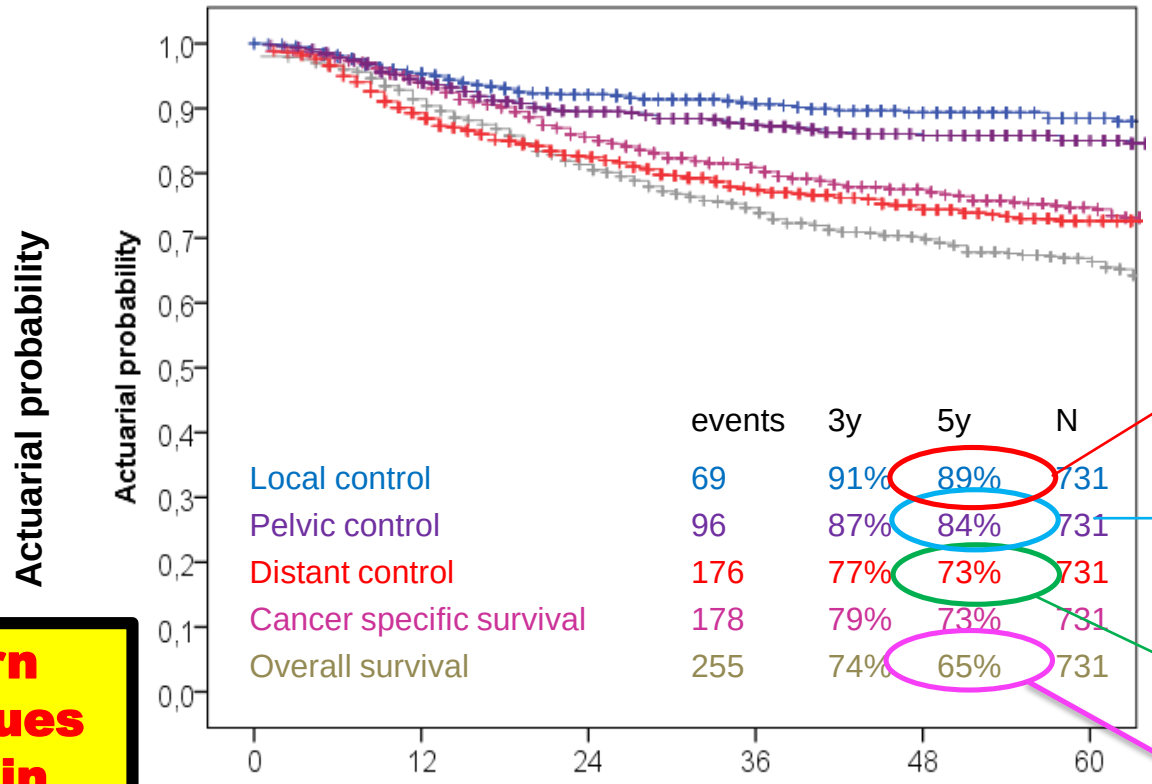


3D dose planning



Dose delivery

RetroEMBRACE: Outcome



	events	3y	5y	N
Local control	69	91%	89%	731
Pelvic control	96	87%	84%	731
Distant control	176	77%	73%	731
Cancer specific survival	178	79%	73%	731
Overall survival	255	74%	65%	731

11%

16%

27%

35%

Modern techniques result in very good tumour control and survival

Months

LC	731	603	491	384	294	187
PC	731	603	491	384	294	187
DC	731	603	491	384	294	187
CSS	731	651	537	429	332	220
OS	731	651	537	429	332	220

MEDIZINISCHE UNIVERSITÄT WIEN

Pattern of Relapse

COMPREHENSIVE CANCER CENTER VIENNA

Sturdza et al. Radiotherapy Oncology, 2016

Late side effects

- Can occurr at any time after the completion of treatment
- Are more frequent in locally advanced cancers treated with curative intent (i.e cervical cancer)
- In severe cases may require treatment/intervention
- Many could be prevented through appropriate supportive care

Overview: Gastro-intestinal

-maximum incidence of individual bowel symptoms

CTCAE 3.0	Diarrhea	Flatulence	Incontinence	Stenosis	Fistula
Grade 0					
Baseline	1023 (95%)	992 (92%)	1066 (99%)	1078 (99%)	1077 (99%)
Max FUP	568 (58%)	592 (61%)	840 (86%)	947 (98%)	963 (99%)
Grade 1					
Baseline	48 (5%)	70 (7%)	13 (1%)	1 (0.01%)	2 (0.02%)
Max FUP	319 (33%)	299 (31%)	108 (11%)	11 (1%)	1 (0.1%) *
Grade 2					
Baseline	7 (0.6%)	17 (2%)	0	0	0
Max FUP	**71 (7%)**	**81 (8%)**	**20 (2%)**	**4 (0.4%)**	**2 (0.2%)**
Grade ≥3					
Baseline	1 (0.1%)		0	0	0
Max FUP	**14 (1%) (1 G5)**		**4 (0.4%)**	**10 (1%) (4 G4)**	**6 (0.6%) (3 G4)**

*G1 morbidity increases significant compared to baseline

Diarrhea, bloating, fecal urgency and incontinence occur to some degree in 1/3 of patients, but severe side effects happen in less than 2 %

EMBRACE

Jensen et al, ESTRO 2017

Bladder and urinary toxicity 970 patients

	Frequency	Incontinence	Spasm	Bladder contracture	Ureter stenosis	Cystitis	Bleeding	Fistula
G0	482 (47.7%)	643 (66.3%)	898 (97.9%)	964 (92.6%)	930 (95.9%)	797 (82.2%)	916 (94.4%)	957 (98.7%)
G1	378 (30.0%)	225 (23.2%)	58 (6.0%)	58 (6.0%)	10 (1.0%)	109 (11.2%)	41 (4.2%)	3 (0.3%)
G2	96 (9.9%)	86 (8.9%)	13 (1.3%)	13 (1.3%)	9 (0.9%)	57 (5.9%)	11 (1.1%)	2 (0.2%)
G3	14 (1.4%)	12 (1.2%)	1 (0.1%)	1 (0.1%)	18 (1.9%)	5 (0.6%)	2 (0.2%)	5 (0.5%)
G4		4 (0.4%)	0 (0%)	0 (0%)	3 (0.3%)	1 (0.1%)	0 (0%)	3 (0.3%)

* 7 patients had tumor involvement of the bladder at time of diagnosis

Frequency, painful urination, cystitis and incontinence occur to some degree in 1/3 of patients, but severe side effects happen in less than 2 %

Fokdal et al, 2016

Vaginal symptoms

N=767	Vaginal dryness	Vaginal stenosis	Vaginal mucositis	Vaginal bleeding	Vaginal fistula	Other vag. symptoms
G0	395 (51%)	287 (37%)	529 (69%)	498 (65%)	753 (98%)	671 (88%)
G1	328 (43%)	339 (44%)	199 (26%)	259 (34%)	5 (1%)	74 (10%)
G2	44 (6%)	128 (17%)	33 (4%)	9 (1%)	1	17 (2%)
G3		12 (2%)	5 (1%)	1	5* (1%)	4
G4			1	0	1*	0

Vaginal dryness, narrowing, painful intercourse, discharge occur to some degree in 1/2 of patients, but severe side effects happen in less than 4 %

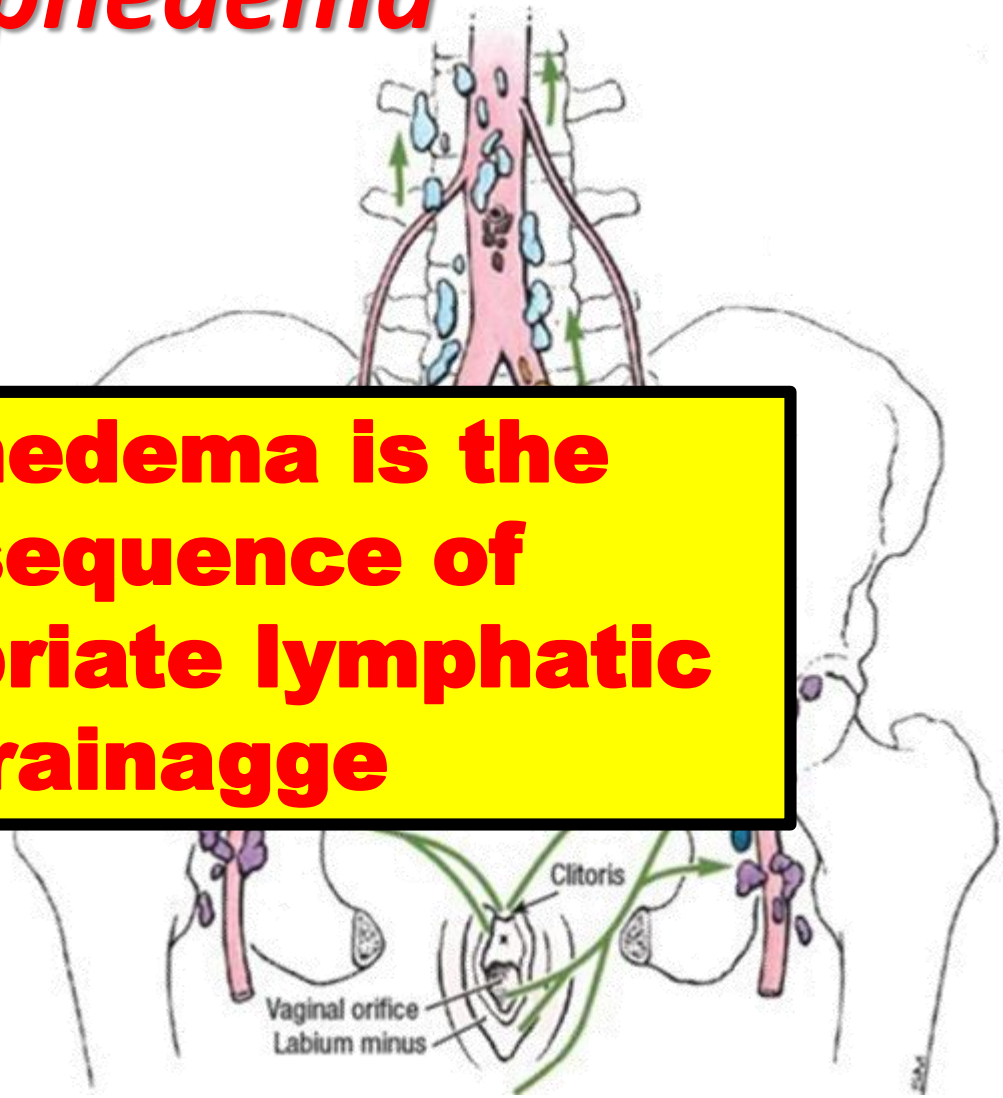
* 2 vesico-vaginal
1 uretero-vaginal
1 recto-vaginal
2 vesico+recto-vaginal

Courtesy of Kathrin Kirchheiner, 2017

Lymphedema

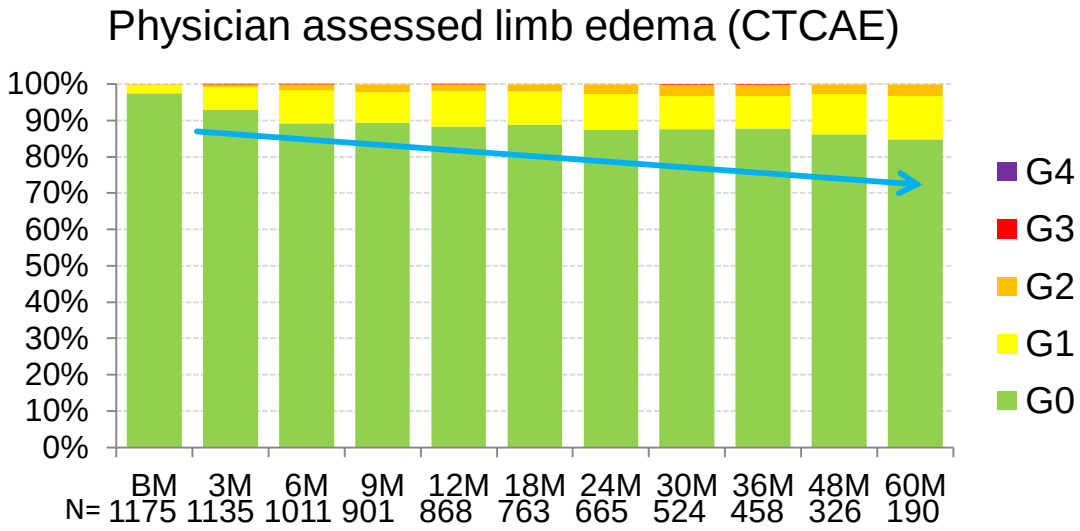
- Lymphedema is a collection of fluid that causes swelling in the arms and legs
- Without normal lymph drainage, fluid can build up in the affected arm or leg, and lymphedema can develop
- Medication such as Tamoxifen, radiation therapy, surgery and injury to the lymph nodes can also cause lymphedema

Lymphedema



Lymphedema is the consequence of innapropriate lymphatic drainagge

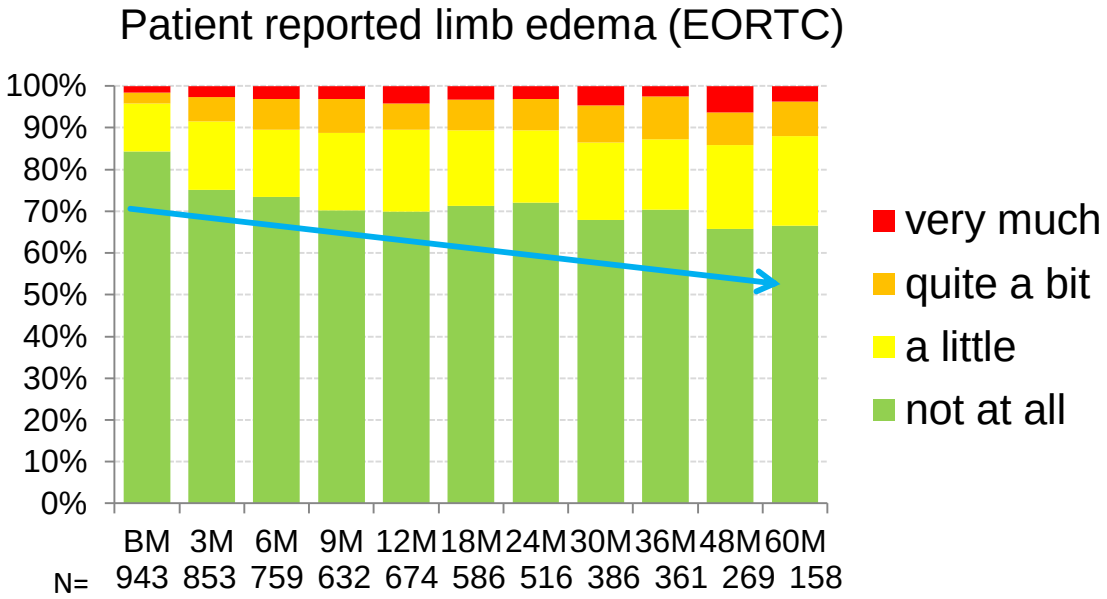
Frequency of Lymphoedema 1176pts, FU 27 months



G2: >10–30% inter-limb discrepancy in volume or circumference

G1: 5 – 10% inter-limb discrepancy in volume or circumference

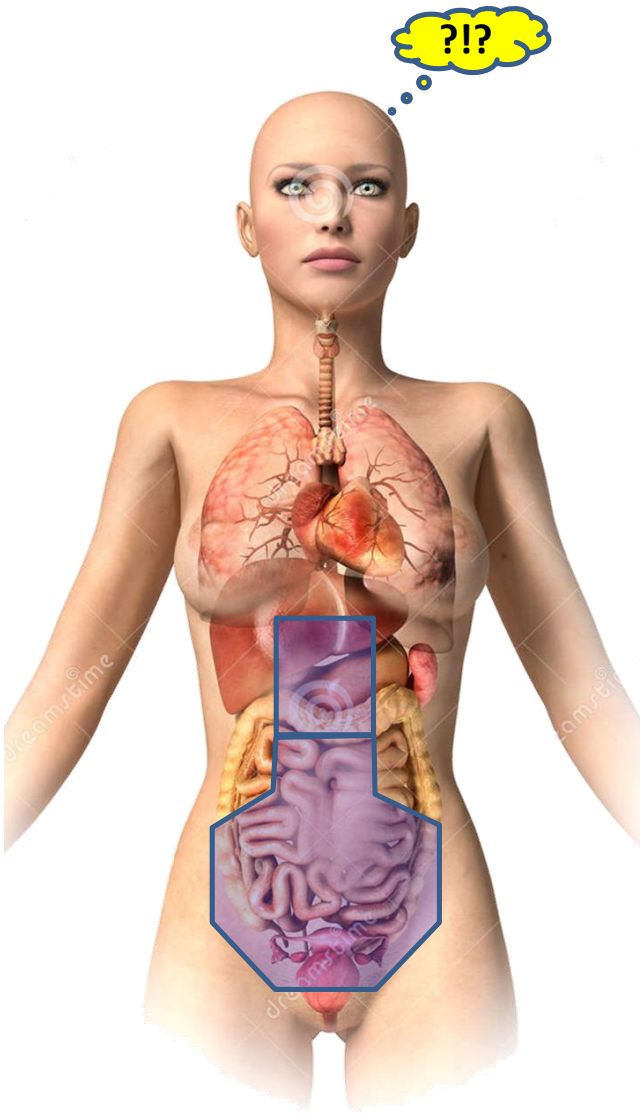
Progressive manifestation pattern over time

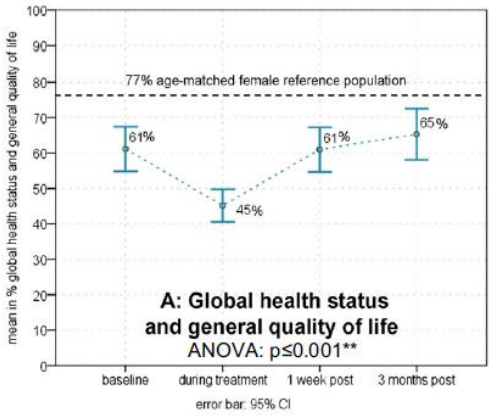


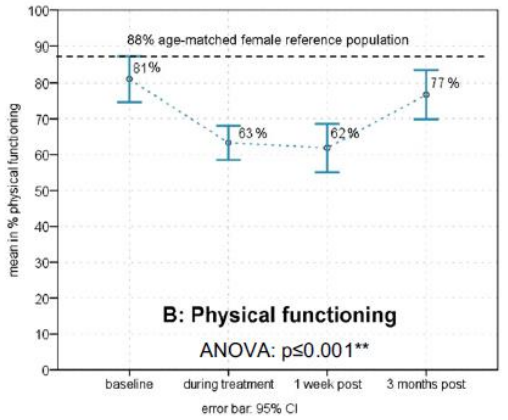
Najjari D. &al, ESTRO 2017

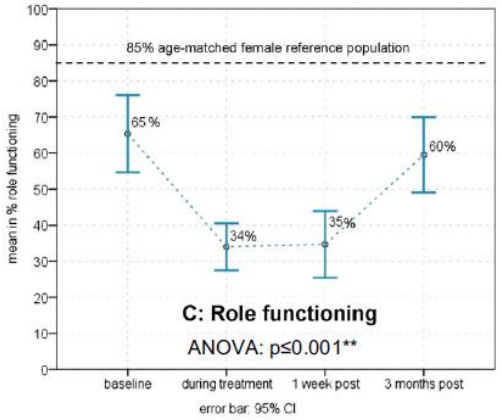
Severe and moderate lymphedema occurrs very rarely (5%) significantly increased by preexisting comorbidities, higher body mass index, invasive lymph node staging, previous abdominal/inguinal surgery and extended radiation fields

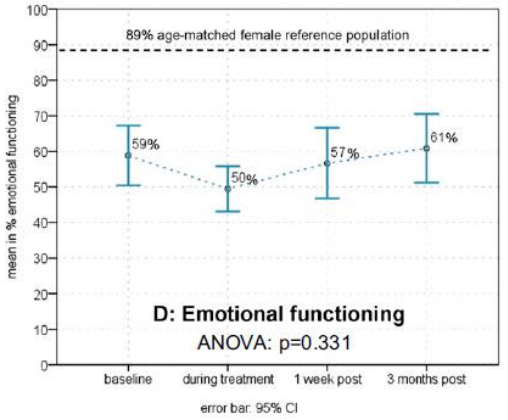
Side effects of Radiation: Human factor

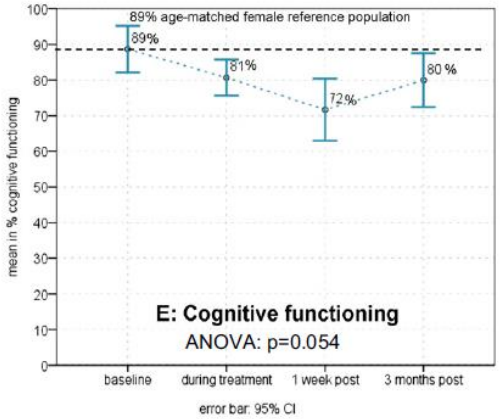


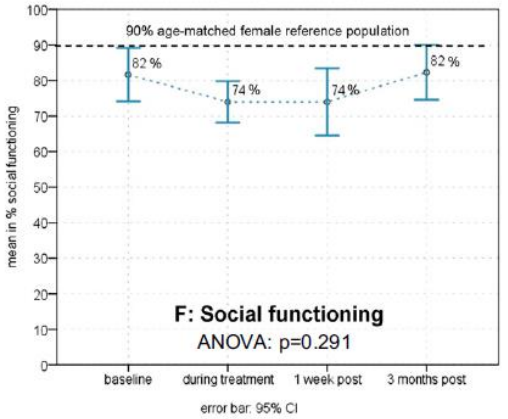












Kirchheiner et al/Gynecologic Oncology, 2015

Psychosocial consequences of cancer treatment are transient and QoL improves after a while in the majority of patients

Conclusion

- Radiation treatment of gynecologic cancer can cause long-term side effects impacting to some degree on the quality of life of patients
- While 1/3 to ½ of patients may develop some kind of long term toxicity, severe toxicity is very rare
- In some gynecological malignancies, the benefit of Radiation treatment may outweight the limited toxicity (i.e Cervical cancer)
- Future research is aiming to improve the outcome while decreasing the toxicity profile

Conclusion: multidisciplinary team work is needed

alina.sturdza@meduniwien.ac.at