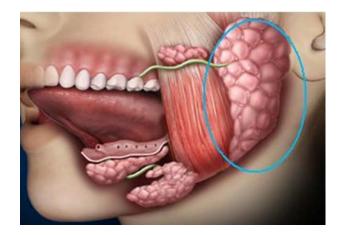




Role of Radiotherapy in Salivary Gland Tumors



Dr. Monali Swain Associate Professor Department of Radiation Oncology Head and Neck Disease Management Group Tata Memorial Hospital







I have nothing to disclose.



Introduction



- About 0.4% of all cancers, <5% of head and neck cancers
- Benign tumours: More in females, younger age (mean age 46 years)
- Malignant tumours: equal in both sexes, older age (mean age 54 years)

	% Of tumours	% Malignant
Parotid	70%	25%
Submandibular	8%	43%
Minor glands	22%	65%



5th WHO Classification of Salivary Gland Tumors



Non-neoplastic epithelial lesions

- Nodular oncocytic hyperplasia
- Lymphoepithelial sialadenitis

Benign epithelial tumours

- Pleomorphic adenoma
- Basal cell adenoma
- ➢ Warthin tumour
- Oncocytoma
- Salivary gland myoepithelioma
- Canalicular adenoma
- Cystadenoma of the salivary glands
- Ductal papillomas
- Sialadenomapapilliferum
- Lymphadenoma
- Sebaceous adenoma
- Intercalated duct adenoma and hyperplasia
- Striated duct adenoma
- Sclerosing polycystic adenoma
- Keratocystoma

Malignant epithelial tumours

- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Acinic cell carcinoma
- Secretory carcinoma
- Microsecretory adenocarcinoma
- Polymorphous adenocarcinoma
- Hyalinizing clear cell carcinoma
- Basal cell adenocarcinoma
- Intraductal carcinoma
- Salivary duct carcinoma
- Myoepithelial carcinoma
- Epithelial-myoepithelial carcinoma

Mucinous adenocarcinoma

- Sclerosing microcystic adenocarcinoma
- Carcinoma ex pleomorphic adenoma
- Carcinosarcoma of the salivary glands
- Sebaceous adenocarcinoma
- Lymphoepithelial carcinoma
- Squamous cell carcinoma
- Sialoblastoma

>

Salivary carcinoma NOS and emerging entities

Mesenchymal tumours specific to the salivary glands

Sialolipoma



Management Challenging

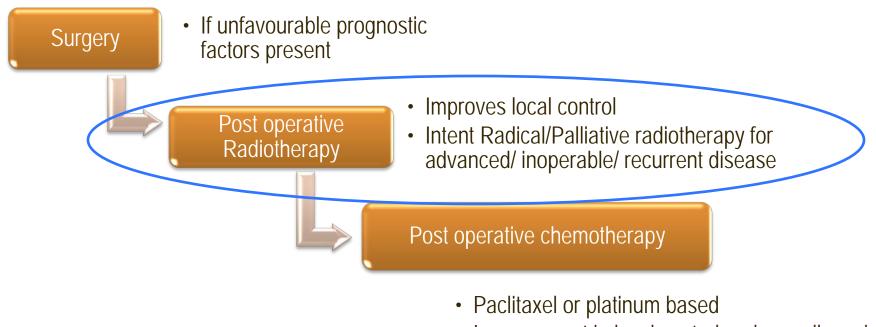


- Varied histology and biologic behavior.
- Limited clinical trial data.
- Decision for optimal treatment is challenging.
- Best decided in the context of a multidisciplinary tumor board.



Management





Improvement in local control and overall survival ?



Role of Radiotherapy



- Post-op Radiotherapy
- Definitive Radiotherapy
- Palliative radiotherapy
- Radiotherapy in recurrent salivary gland cancers

CLINICAL INVESTIGATION

RECURRENT PLEOMORPHIC ADENOMA OF THE PAROTID GLAND: LONG-TERM OUTCOME OF PATIENTS TREATED WITH RADIATION THERAPY

Non-Control HOSPITC

Allen M. Chen, M.D.,* Joaquin Garcia, M.D.,[†] M. Kara Bucci, M.D.,* Jeanne M. Quivey, M.D.,* and David W. Eisele, M.D.[‡]

- Retrospective, n= 34 (25% 1st recurrence, 75% 2nd or more recurrence)
- Median Follow up 17.6yrs.
- RT given to entire parotid bed with 2-3 cm margins, with wedged-pair technique (56%) or photon-electron combination (44%) to a dose of 45-59.4 Gy (median 50 Gy) at 1.8-2 Gy daily, no IMRT used

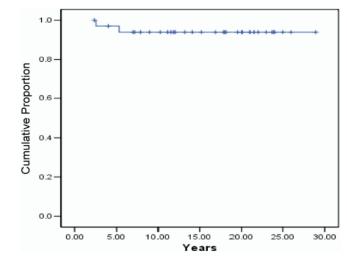


Fig. 1. Local control of all patients treated with postoperative radiation therapy for recurrent pleomorphic adenoma.

20yr actuarial local control 94% (Reported local control for surgery alone was 65-85% for first recurrences and 30-50% for second recurrences)

Head and Neck



The role of adjuvant radiotherapy in management of recurrent pleomorphic adenoma of the parotid gland: a systematic review



Laura Mc Loughlin^{1,2} · Sarah Louise Gillanders² · Susan Smith¹ · Orla Young²

2019

Abstract

European Archives of Oto-Rhino-Laryngology

Purpose Recurrent pleomorphic adenoma poses a significant treatment challenge, considering its propensity for further recurrence and potential for malignant transformation. The role of adjuvant radiotherapy in its management is widely debated. The aim of this study was to determine whether adjuvant radiotherapy is more effective than surgical resection alone in patients with recurrent pleomorphic adenoma of the parotid gland, in terms of further recurrence, malignant transformation and treatment-related complications.

Methods Using PRISMA guidelines, a systematic review comparing adjuvant radiotherapy with surgery alone in the treatment of recurrent pleomorphic adenoma was conducted. Pubmed, OVID, EBSCO, Embase, The Cochrane Library, SCOPUS and OpenGrey databases from 1988 to 2018 were searched. Quality analysis was carried out using the Newcastle–Ottawa Scale and narrative synthesis used to summarise results.

Results Of 891 records screened, eight studies were included, assessing 366 participants. Two noted a benefit of adjuvant radiotherapy in reducing further recurrence. The remainder did not show significant benefit, although four showed a trend towards lower rates. Only one case of malignant transformation was identified in a patient not irradiated. Similar rates of facial nerve dysfunction were identified between groups.

Conclusion The available evidence suggests that adjuvant radiotherapy reduces recurrence rates in patients with recurrent pleomorphic adenoma and certain adverse prognostic factors. While it appears not to have significant adverse effects, given the lack of prospective evidence, we recommend careful use in patients at high risk of further recurrence and further research in the form of well-designed randomised controlled trials.



4N0(P5.047), pTanyN1(P<.001)

Patterns of Care and Survival of Adjuvant Radiation for Major Salivary Adenoid Cystic Carcinoma



Anna Lee, MD, MPH; Babak Givi, MD; Virginia W. Osborn, MD; David Schwartz, MD; David Schreiber, MD Larvngoscope 127: September 2017 NCDB study, 1784 patients Whole Cohor Positive Margins 73.6% received adjuvant RT ."+Surgery alone surperv alone 0.8 Median F/U 47.5 months ····· roportion alive 0.6 0.6p<0.001 5yr OS: 72.5% in Sx alone arm p=0.001 0.4-82.45 in Sx+RT arm 0.2* PORT beneficial in presence of positive \succ margins. 0.0* 12.00 24.00 36,00 48 00 72.00 84.00 12:00 24.00 36,00 48.00 60,00 72.00 84.00 96.00 Survival time (months) Benefit in pT1-2N0 (P<.001), pT3-</p> Survival time (months)

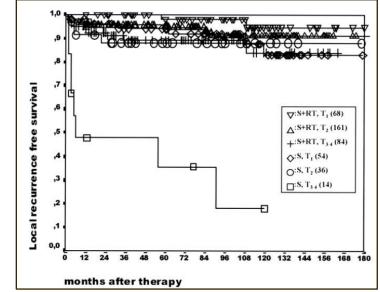
PORT is beneficial in all stages of ACC



THE ROLE OF RADIOTHERAPY IN THE TREATMENT OF MALIGNANT SALIVARY GLAND TUMORS

Chris H. J. Terhaard, M.D., Ph.D.,* Herman Lubsen, M.D., Ph.D.,[†]
Coen R. N. Rasch, M.D., Ph.D.,[‡] Peter C. Levendag, M.D., Ph.D.,[§]
Hans H. À. M. Kaanders, M.D., Ph.D.,[∥] Reineke E. Tjho-Heslinga, M.D.,[¶]
Piet L. A. van Den Ende, M.D.,[#] Fred Burlage, M.D.,^{**} on behalf of the Dutch Head and Neck Oncology Cooperative Group (NWHHT)

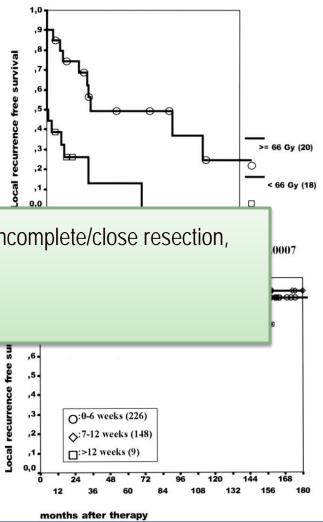
- Retrospective analysis of 538 patients.
- 386 surgery plus adjuvant RT, 112 surgery alone, 40 definitive RT.
- Significant Improvement of 10 yr LC over surgery alone
 - ✓ T3-T4 tumours (84 versus 18%)
 - ✓ Close (<5 mm) resection margin(95 versus 55%)
 - ✓ Incomplete resection (82 versus 44%)
 - ✓ Bone invasion (86 versus 54%)
 - ✓ Perineural invasion (88 versus 60%)





Results

- Adjuvant RT significantly improved LRC in pN+ neck (86 vs 62% for surgery alone). Marginal dose–response favouring >46 Gy
 - Adjuvant RT dose at least 60 Gy indicated for T3-4 tumours, incomplete/close resection, bone invasion, PNI, pN+
 - ✓ At least 66 Gy should be given for unresectable tumours.
- Local control showed no relation with interval between surgery and adjuvant RT (median 6 weeks)





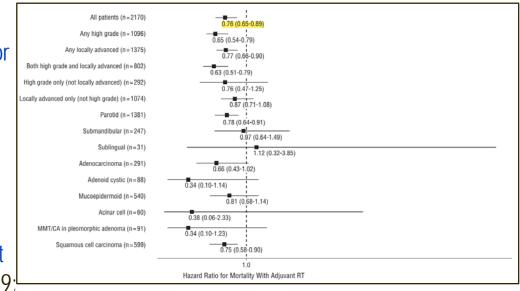
Adjuvant Radiation Therapy for High-Grade and/or Locally Advanced Major Salivary Gland Tumors



Usama Mahmood, MD; Matthew Koshy, MD; Olga Goloubeva, PhD; Mohan Suntharalingam, MD

- SEER database study, n=2170, 1988-2005.
- High grade T3/T4 advanced malignant major salivary gland malignancy.
- 72% adjuvant RT (young ,higher T and N category), 28% surgery alone.
- Significantly improved survival with adjuvant RT (HR for mortality, 0.76; 95% CI, 0.65-0.89; P.001)

ARCH OTOLARYNGOL HEAD NECK SURG/VOL 137 (NO. 10), OCT 2011





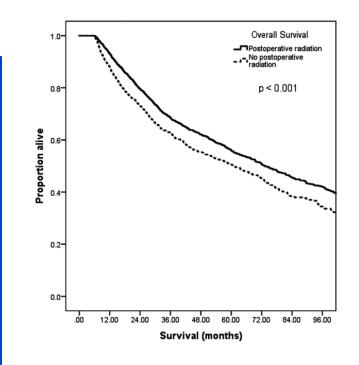
Impact of Adjuvant Radiotherapy for Malignant Salivary Gland Tumors

Joseph Safdieh, MD^{1,2,3}, Babak Givi, MD^{4,5}, Virginia Osborn, MD^{1,2}, Ariel Lederman, MD^{1,2}, David Schwartz, MD^{1,2}, and David Schreiber, MD^{1,2}

- NCDB study, 2004-2012, 4068 patients.
- 67.1% received adjuvant RT, 32.9% Sx alone.
- Median F/U 49.1 months
- Use of adj RT (hazard ratio, 0.78; 95% CI, 0.71-0.86; P < 0.001) and female sex was associated with improved survival in multivariable analysis.

Otolaryngology– Head and Neck Surgery 2017, Vol. 157(6) 988–994



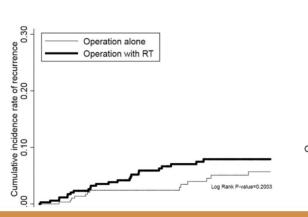


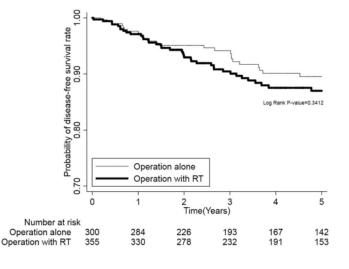


Adjuvant RT in Early SGC The effect of adjuvant radiotherapy on clinical outcomes in early major salivary gland cancer

Wei-Ju Hong MD¹ | Shih-Lun Chang MD^{2,3} | Chia-Jen Tsai MD¹ | Hung-Chang Wu MD^{4,5} | Yi-Chen Chen MS⁶ | Ching-Chieh Yang MD, PhD^{1,5} Chung-Han Ho PhD^{6,7}

- N=655 patients
- Adjuvant RT: 355 (54.2%)
- Surgery Alone: 300 (45.8%)
- Only major SGC





In early stage major SGC, adjuvant radiation therapy was not associated with improved locoregional recurrence and DSS, even for those with high-risk histopathological factors.

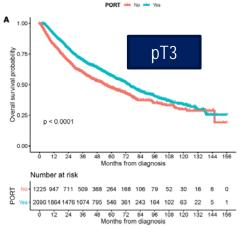


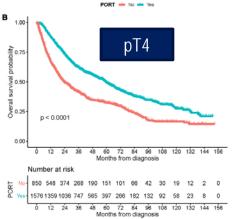
Prediction model to estimate overall survival benefit of postoperative radiotherapy for resected major salivary gland cancers

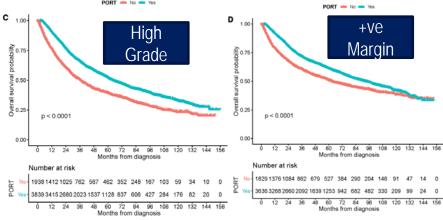
Corbin D. Jacobs ^a, Ian Barak ^b, Sin-Ho Jung ^b, Daniel J. Rocke ^c, Russel R. Kahmke ^c, Gita Suneja ^d, Yvonne M. Mowery ^{c, e, *}



- To develop and validate a prediction model to estimate overall survival (OS) with and without postoperative radiotherapy (PORT) for resected major salivary gland (SG) cancers.
- N= 18,400; 9,721 (53%) received PORT
- 86% parotid, 13% submandibular, and 1% sublingual
- PORT was significantly associated with improved OS in pT3 (p < 0.001), pT4 (p < 0.001), high grade (p < 0.001), node-positive (p < 0.001), and positive margin (p < 0.001).







Multivariate Cox model for overall survival

Variable	Hazard ratio	95% confidence interval	P-value
PORT			< 0.001
For pT1	1.03	0.86-1.24	0.745
For pT2	0.83	0.74-0.94	0.003
For pT3	0.68	0.68-0.74	< 0.001
For pT4	0.55	0.48-0.62	< 0.001
Age at diagnosis (units $= 10$			< 0.001
years)	1.52	1.45-1.60	< 0.001
No PORT	1.37	1.31-1.42	< 0.001
PORT			
Male (ref: female)	1.28	1.17-1.39	< 0.001
Charlson-Deyo comorbidity score	1.22	1.15-1.30	< 0.001
Primary site (ref: parotid)			< 0.001
Submandibular	1.32	1.17-1.49	< 0.001
Sublingual	0.72	0.40-1.49	0.278
Pathologic T-stage	-	-	< 0.001
Ratio of nodal positivity	1.29	1.25-1.34	< 0.001
Tumor grade	1.34	1.25-1.43	< 0.001
Positive surgical margin (ref: negative)	1.26	1.17–1.37	<0.001

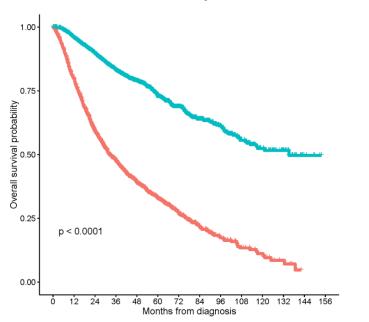
Other factors affecting survival:

- Older age at diagnosis,
- Male sex,
- Higher Charlson-Deyo comorbidity index,
- Non-sublingual gland primary tumor,



Model Development

Risk Score 📥 High 📥 Low



https://www.mdcalc.com/saliv ary-gland-cancer-model-survival-postoperative-radiotherapy-port.





Elective Neck Treatment



- Adenoid cystic carcinoma, high-grade.
- Invasive carcinoma ex-pleomorphic adenoma.
- High-grade adenocarcinoma high-grade adenocarcinoma not otherwise specified (NOS)
- Salivary duct carcinoma
- High-grade acinic cell carcinoma.



PATTERNS OF NODAL RELAPSE AFTER SURGERY AND POSTOPERATIVE RADIATION THERAPY FOR CARCINOMAS OF THE MAJOR AND MINOR SALIVARY GLANDS: WHAT IS THE ROLE OF ELECTIVE NECK IRRADIATION?



Allen M. Chen, M.D.,* Joaquin Garcia, M.D.,[†] Nancy Y. Lee, M.D.,[‡] M. Kara Bucci, M.D.,[§] and David W. Eisele, M.D.,^{\parallel}

- Retrospective, n=251,cN0 neck and no neck dissection who received adjuvant RT
- 52% (131 patients) received ENI (I/L in 90 and B/L in 41 patients)
- Dose 40-66 Gy, median 50 Gy, to level II to IV.
- M/C sites of nodal recurrence- I/L level I and level II
- No C/L neck recurrences
- No difference in10 yr nodal faillures for major and minor salivary gland tumours, 11% vs 14%

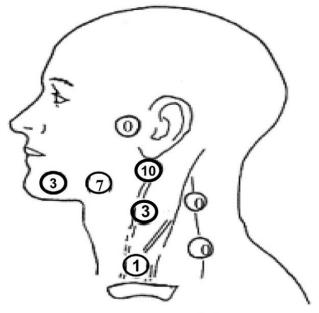
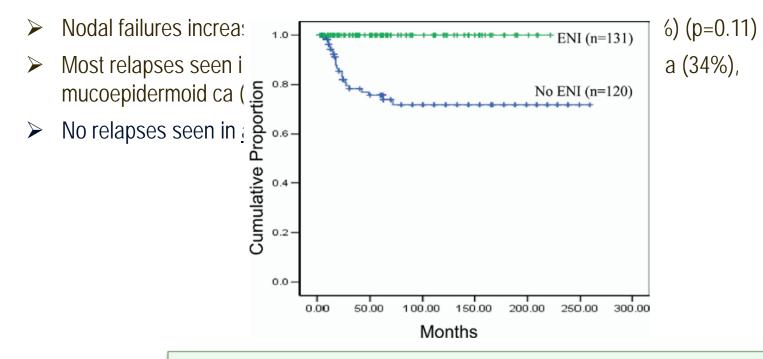


Fig. 2. Pattern of nodal relapse (ipsilateral neck).







10 yr nodal relapse 0% with ENI, 26% without ENI Conclusion: ENI prevents nodal relapse and should be considered for patients with high risk of regional failure.



Elective Neck Treatment for Clinically Node-Negative Salivary Gland Cancer: Observation, Neck Dissection, or Neck Irradiation?



E. Ilori, B. Hair, L. Rybicki, B.B. Burkey, J.L. Geiger, E. Lamarre, B. Prendes, J. Ku, D. Chute, C. Griffith,

N.M. Woody, S. Koyfman and S.R. Campbell

International Journal of Radiation Oncology, Biology, Physics, 2022-04-01, Volume 112, Issue 5, Pages e17-e17,

- Retrospective audit, IRB approved, n=445
- No difference in LRC between END or ENI.
- The END+ENI group had low LRR despite poor prognostic factors and the highest incidence of distant metastasis and lowest survival.

	None (n= 203)	END (n=83)	ENI (n=71)	END+ENI (n=88)	P value
cT3/T4	15.8%	21.7%	32.4%	42.1%	< 0.001
pT3/T4	21.6%	33.7%	56.2%	75%	< 0.001
Positive margin	28.2%	19.2%	54.4%	41.2%	< 0.001
Borderline nodal features	4.9%	9.6%	7%	22.7%	<0.001
Poor differentiation	10.9%	33.7%	36.2%	60.9%	<0.001
PNI	23.3%	36.7%	46.8%	78%	< 0.001
LVSI	9.4%	21.8%	24.6%	50.6%	< 0.001
ENE	1.5%	7.4%	5.9%	26.8%	< 0.001
Local recurrence	13.3%	10.8%	8.5%	9.1%	0.6
Regional recurrence	3.9%	6%	5.6%	4.5%	0.76
Distant metastasis	6.4%	14.5%	25.4%	30.7%	<0.001



Indications of Adjuvant RT



• Benign: Recurrent Pleomorphic Adenoma

Malignant:

- 1. Microscopically positive or close (<5 mm) surgical margins
- 2. Large tumours (T3 or T4 disease) requiring radical resection
- 3. Intermediate/High tumour grade
- 4. Involvement of skin, bone, nerve (gross invasion or extensive PNI)
- 5. Tumour extension beyond the capsule of the gland with periglandular and soft tissue invasion
- 6. Lymph node metastases
- 7. Gross residual disease



Target Volume Delineation



Pre-Requisites

- Preoperative imaging
- Operative notes
- Surgical pathology reports
- Postoperative imaging including CT simulation
 High Dose Target: Salivary gland surgical bed and involved nodal levels Dose: 60Gy/30#

Elective Nodal Volume: Dose: 54Gy/30#

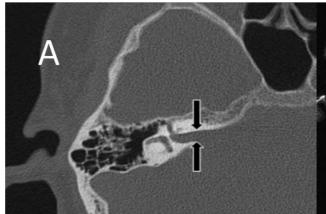


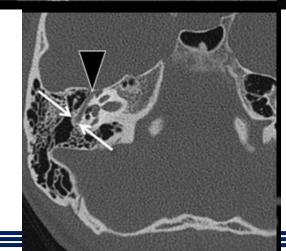
Special Consideration



- In case of deep lobe parotid cancer, the infratemporal fossa and the parapharyngeal space should be included in the field.
- In case of PNI, nerve pathway to skull base should be delineated.
- Always cover CNVII to stylomastoid foramen for parotid tumor.
- For gross involvement of CNVII, cover petrous bone and formen ovale (due to connections with CNV3)

KO HC,2014; Practical Radiation Oncology

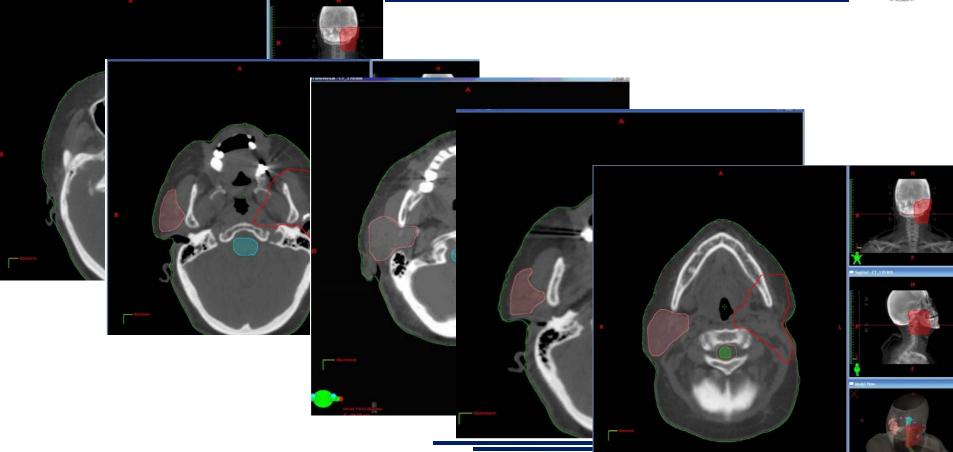






UK COSTAR Guidelines







Steps of Planning



- 1. Pre planning
- 2. Consent & Counselling
- 3. Simulation
- 4. Contouring
- 5. Planning (Conventional / Conformal)
- 6. Plan Evaluation
- 7. Plan implementation



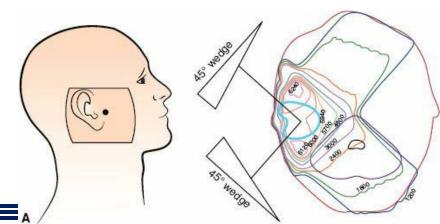
Radiotherapy Technique Conventional Photon



Patient positioning

- □ Supine/face turned to one side
- Arms by side
- Accessories / Immobilisation
- Baseplate
- Neutral neck rest (NNR1 / NNR5)
- 4 clamp thermoplastic sheet
- using bolus (If required)
- Laser points marked at level of Glabella Lead markers placed at Laser points
- 2.5mm CT cuts to be taken from 2cm above vertex to carina

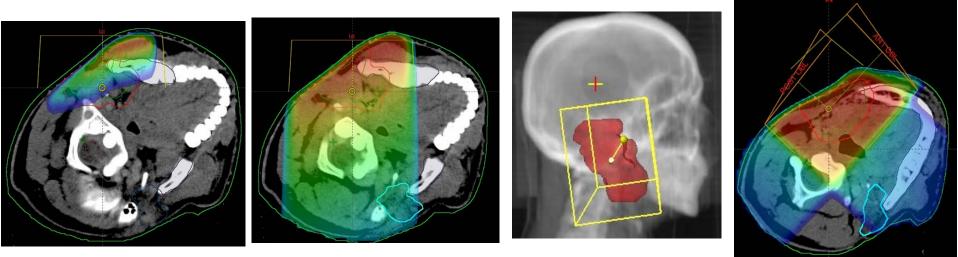






Fields for Conventional Planning





Direct Photon Field

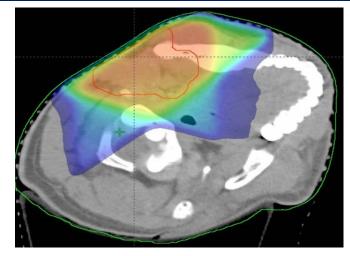
Wedge pair Portal

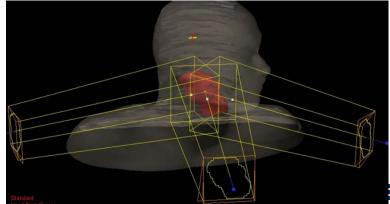


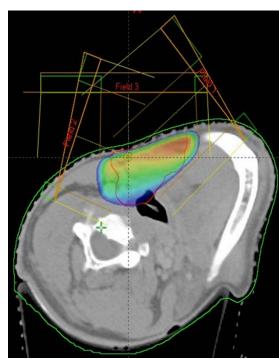
Conformal 3DCRT Technique



- Much better sparing of normal tissue than conventional technique.
- Better Target Coverage



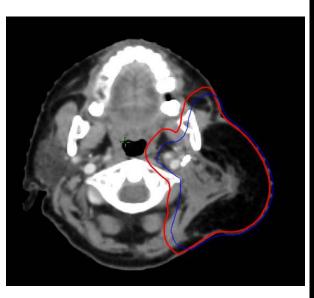


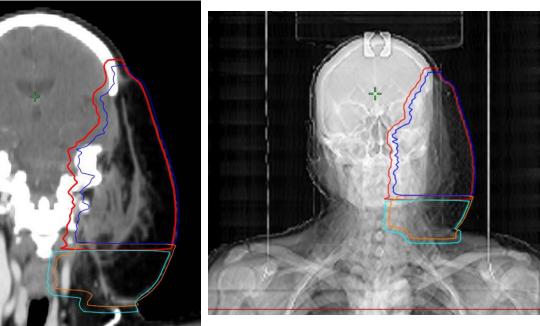








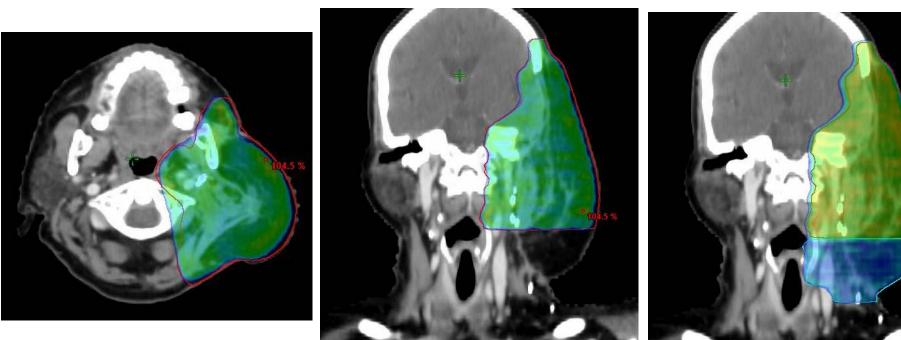






Dose Distribution

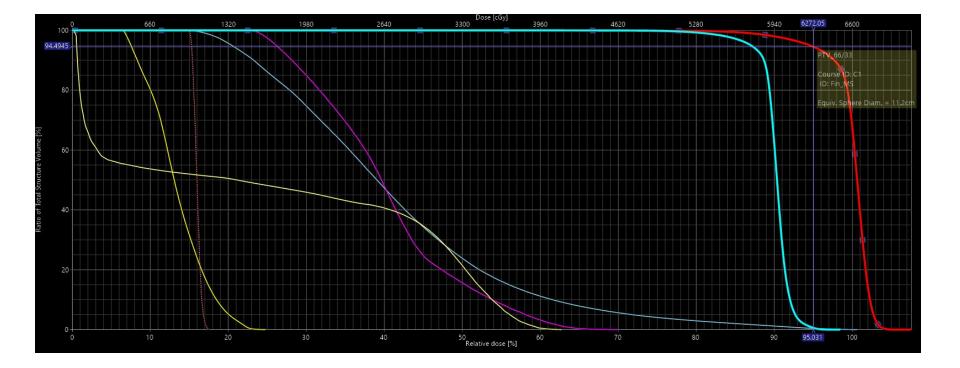








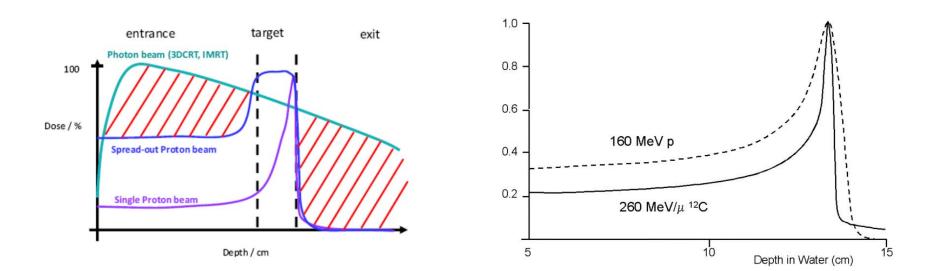






Charged Particle Therapy





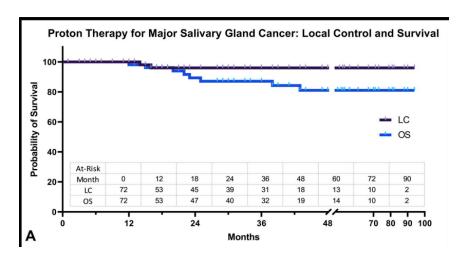
Sharp increase of the dose at well defined depth Rapid fall off beyond that point

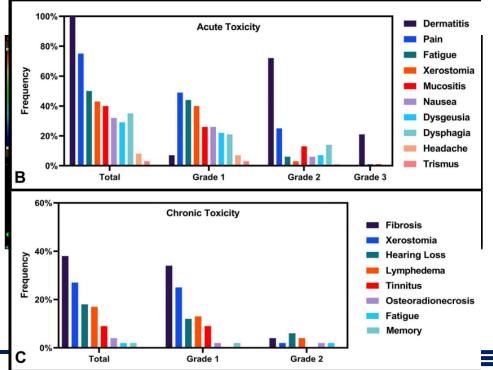


Proton Therapy for Major Salivary Gland Cancer: Clinical Outcomes

STUDIEL HOSPIAL

Alexander N. Hanania, MD, MPH^{1,2}; Xiaodong Zhang, PhD³; G. Brandon Gunn, MD²; David I. Rosenthal, MD²; Adam S. Garden, MD²; C. David Fuller, MD, PhD²; Jack Phan, MD, PhD²; Jay P. Reddy, MD²; Amy Moreno, MD²; Gregory Chronowski, MD²; Shalin Shah, MD²; Noveen Ausat, BA²; Ehab Hanna, MD⁴; Renata Ferrarotto, MD⁵; Steven J. Frank, MD²

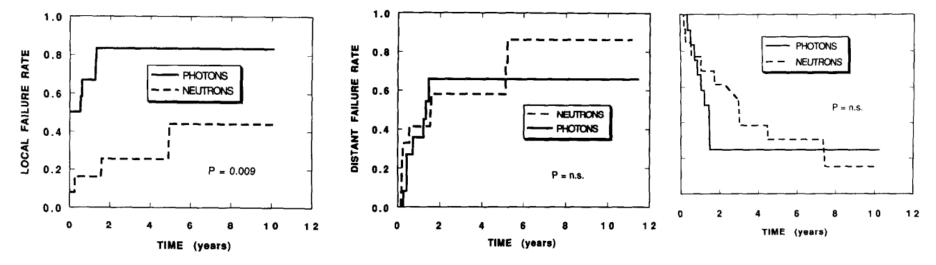






RTOG-MRC Randomized Study Neutron vs Photon





- 10 yr Local Control 56% vs 17%
- Stopped early.
- "Severe" morbidity was greater on the neutron arm, no significant difference in "life-threatening" complications
 IJROBP, 1993



Concurrent chemotherapy or not?



Radiation Therapy With or Without Chemotherapy in Treating Patients With High-Risk Malignant Salivary Gland Tumors That Have Been Removed By Surgery

Study Design	Go to 💌
Study Type 0 :	Interventional (Clinical Trial)
Actual Enrollment 1	252 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Randomized Phase II/Phase III Study of Adjuvant Concurrent Radiation and Chemotherapy Versus Radiation Alone in
	Resected High-Risk Malignant Salivary Gland Tumors
Study Start Date ():	January 2011
Estimated Primary Completion Date ():	October 2023
Estimated Study Completion Date ():	October 2028









Short term: Skin erythema, Mucositis, Dysphagia, Desquamation, Mucosal ulcers

Long term:

- Taste impairment
- Subcutaneous fibrosis
- Xerostomia
- Trismus
- Chronic otitis externa or media
- Hearing loss- conductive of sensori-neural
- Otomastoiditis



Recommendations



Recommendation 3.3

Postoperative RT may be offered to patients with tumors with close margins or intermediate-grade tumors (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Recommendation 3.4

In postoperative cases, the high-dose target should cover the salivary gland surgical bed and appropriate nodal levels (Type: Je evidence based; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 3.5

In the case of perineural invasion, the associated nerve(s) may be covered with an elective or intermediate dose to the skull Radioth base (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: moderate).

Recomm Recommendation 3.6

Postope evidence quality: insufficient; Strength of recommendation: moderate).

Recommendation 3.7

Recommendation store Radiation should be initiated within 8 weeks of surgery (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: moderate).

Recommendation 3.8

Particle therapy, including proton, neutron, and carbon ion therapy, may be used for patients with SGM; there are no indications for the use of heavy particle therapy over photon or electron therapy (Type: evidence based; Evidence quality: low; Strength of recommendation: weak).

Recommendation 3.9

Elective neck irradiation may be offered to patients with cN0 disease for the following indications: T3-T4 cancers or high-grade malignancies (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 3.10

Radiotherapy should be offered to patients with SGM who are not candidates for surgical resection (because of extent of disease or medical comorbidity) (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate). Note. The high-dose target should cover the gross disease in the salivary gland and any appropriate nodal levels.

SPECIAL ARTICLE

Salivary gland cance Solid Cancers (EURA and follow-up[†]

C. van Herpen^{1,2‡}, V. Vander Pooi L. D. Locati¹⁰, A. D. Jensen^{11,12}, L J.-P. Machiels^{20,21}, on behalf of tl

Post-operative or primary RT or chemoradiotherapy

- Post-operative local RT is recommended for T3-T4 and intermediate/high-grade tumours and in cases with close resection margins (1-5 mm; 30×2 Gy), incomplete resection margins (33 \times 2 Gy) or perineural growth [IV, A].
- Post-operative regional RT is recommended for cases
- with pN+ (30 imes 2 Gy) and extranodal extension (33 imes
- 2 Gy). Unilateral ENI (25 \times 2 Gy) is recommended based on the same inclusion criteria as for END [IV, A].
- There is no proof of a beneficial effect of adding ChT to post-operative RT of the primary tumour and neck [IV, C].
- Curative primary RT is indicated for patients with functionally unresectable disease or who are unsuitable for surgery due to comorbidities [IV, B].
- Primary IMRT/VMAT photon RT up to 35×2 Gy to the primary tumour and positive neck nodes with ENI with equal indications as for primary surgery may result in \sim 50% locoregional control [IV, B].
- Primary particle treatment, namely C12, may result in higher locoregional control rates compared with photon RT (but with limited availability) [IV, C].
- There is no proof of a beneficial effect of adding ChT to primary RT in patients with unresectable SGC or those who are unsuitable for surgery [IV, C].



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Take Home



Role	Indications
Adjuvant RT	Intermediate/high grade tumor, T3/T4 stage tumour, PNI+ve, Close /margin +ve LN metastasis.
ENI	High grade and stage tumor.
Volume of ENI	Level I_III
Definitive RT	Residual/recurrent/unresectable tumor
Technique	IMRT should be preferred technique. No indication for particle beam therapy
Dose	Post op: 60-64Gy/30-32# Radical: 66-70Gy/33-35# Elective: 50Gy/25#



HN Radiation Oncology Team





Thank You