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New modalities in the salvage of recurrent nasopharyngeal carcinoma

Dr Jeeve Kanagalingam

FRCS Eng (ORL-HNS)

Department of Otorhinolaryngology

Tan Tock Seng Hospital

SINGAPORE

Tan Tock Seng HOSPITAL

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Nasopharyngeal carcinoma is endemic in Singapore

- Over 93% are of the radiosensitive WHO type III histological variety
- In Chinese men, rates have declined since 1992

Population	Incidence (per 100,000) 1993-97
Hong Kong	21.4
Singapore Chinese	16.3
Shanghai	4.2
NSW, Australia	0.9

Age standardised rates (ASR) in Singapore Chinese men

Period	ASR
1988-1992	18.7
1998-2002	12.5

Source: Singapore Cancer Registry Report No. 6: Trends in Cancer Incidence in Singapore 1968-2002. A Seow et. al.

IMRT - standard of care in Singapore since 2006

- Intergroup 0099 protocol was validated in Singapore in 2005 (J Wee et. al. J Clin Oncol)
- Local results are comparable to other studies in endemic populations

Survival Outcome	1-year	3-year
Overall	98.4%	94.3%
Local recurrence free	96.8%	89.6%
Distant relapse-free	96.8%	89.2%
Disease-free	93.7%	79.0%

Source: Treatment of Nasopharyngeal Carcinoma using Intensity-Modulated Radiotherapy – The National Cancer Centre Singapore Experience. Tham IW et. al. Int J Rad Onc Biol Phys 2009

Locally persistent or recurrent disease is a problem

- 9-40% in most studies
- 10 – 12% with new RT methods
- But 73% of local failures had no evidence of distant or regional disease

Source: Treatment of Nasopharyngeal Carcinoma using Intensity-Modulated Radiotherapy – The National Cancer Centre Singapore Experience. Tham IW et. al. Int J Rad Onc Biol Phys 2009

Recurrence can occur late

N=847 local recurrences

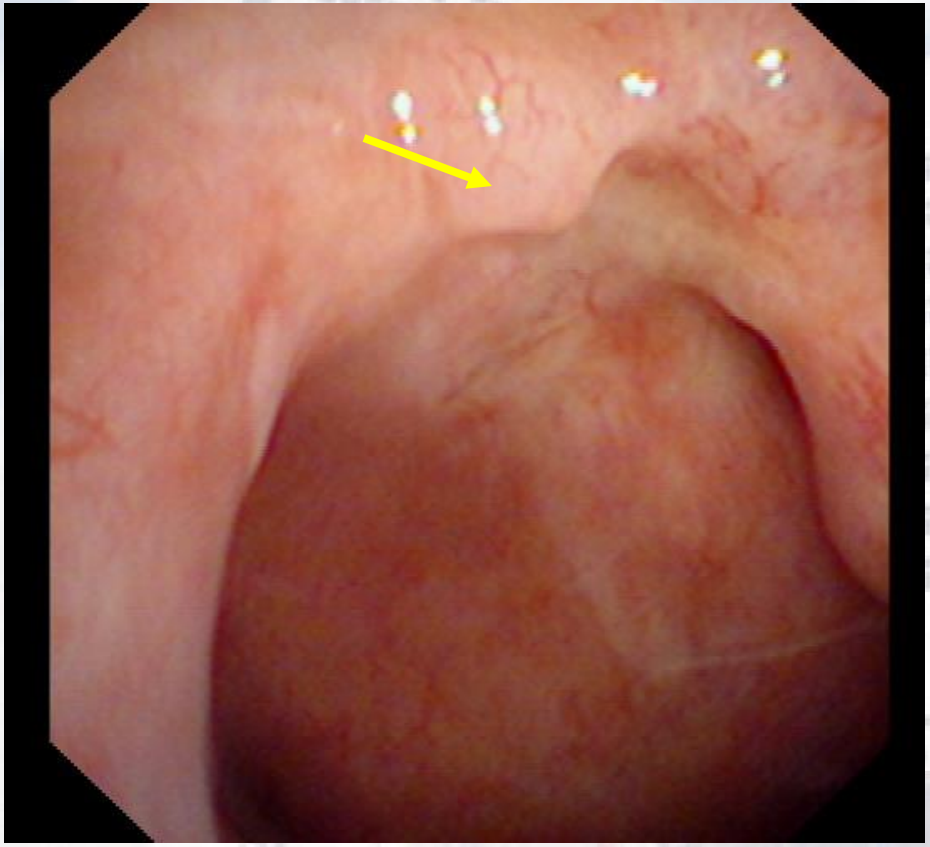
Time post commencement RT	Percentage of local recurrence
> 2 years	52%
2-5 years	39%
>5 years	9%

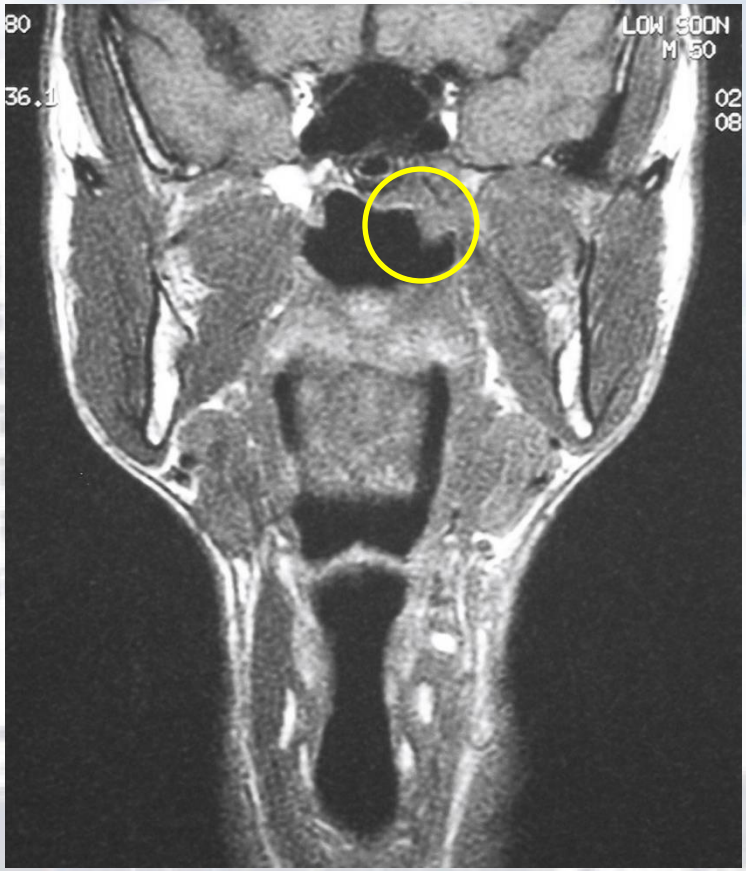
Source: Recurrent nasopharyngeal carcinoma: the puzzles of long latency Lee AW et. al. Int J Rad Onc Biol Phys 1999

New modalities that may make a difference

- Early detection of recurrence
- Radiotherapy
- Surgery

Nasal endoscopy, CT and MRI widely used but not reliable





Nasal endoscopy, CT and MRI widely used but not reliable

Nasal endoscopy in NPC follow-up

	Sensitivity	Specificity	PPV	NPV
Ragab SM (2008)	67%	95%	67%	95%
Kwong DL (2001)	29%	86%	35%	82%

CT and MR in NPC follow-up

	False +	False -
CT	71%	33%
MRI	17%	14%

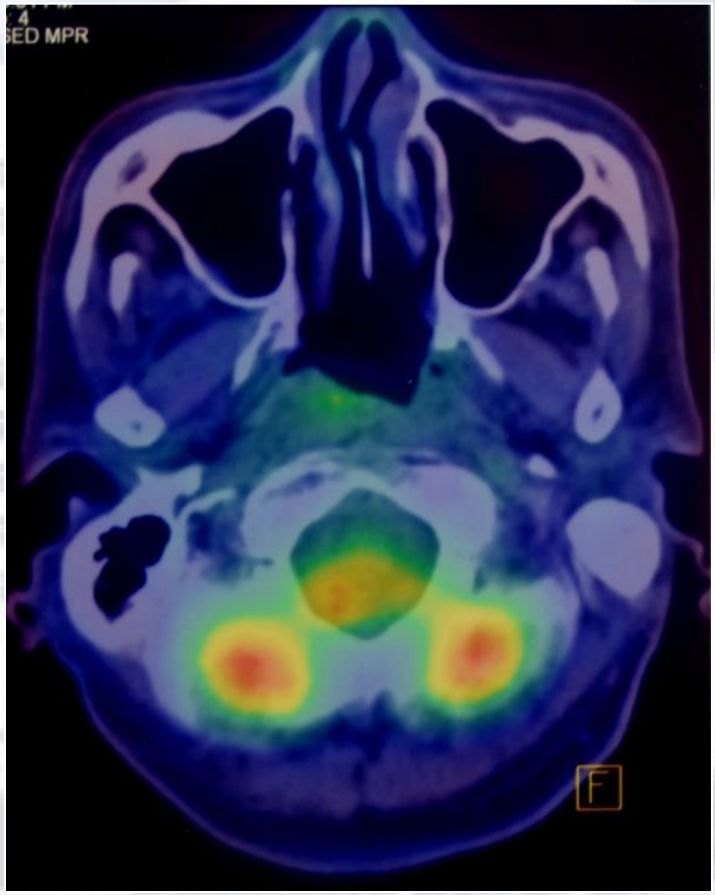
Chong VFH (1997)

FDG-PET/CT offers early detection of recurrence

In a systematic review of 21 studies, PET more sensitive than MR or CT

	CT	MR	PET
Sensitivity	76%	78%	95%

SUV > 4, 3 months post-RT



Source: FDG-PET, CT, MRI for diagnosis of local residual or recurrent nasopharyngeal carcinoma, which one is the best? A systematic review. Liu T et. al. Radiother Oncol 2007

Contact rhinoscopy

- Has been evaluated in irradiated patients
- Diagnostic accuracy of 92.1%
- Correlates well with histology (kappa coefficient=0.847)
- Sensitivity = 100%
- Specificity = 100%

Source: In vivo diagnosis of persistent and recurrent nasopharyngeal carcinoma by contact endoscopy. Pak MW et. al. Laryngoscope 2002

New modalities that may make a difference

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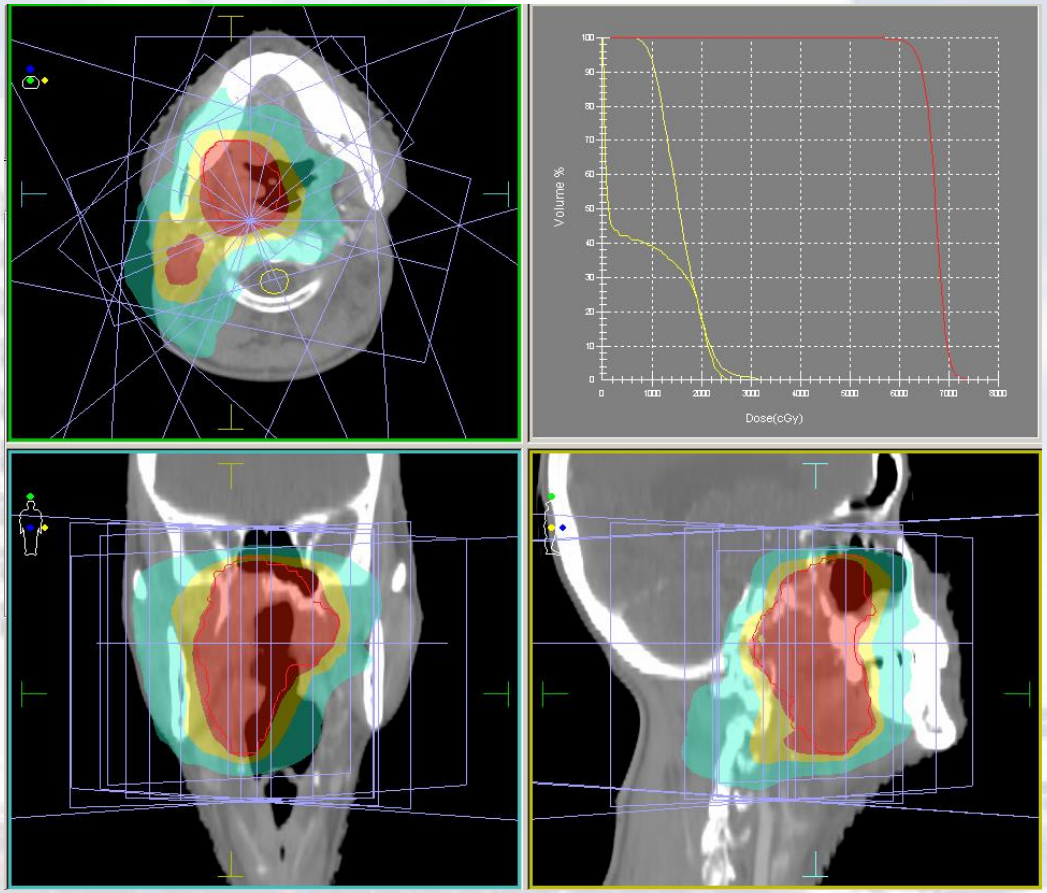
- Surgery

Re-irradiation with IMRT

- Present method of choice in cases not amenable to surgery
- TED > 55-60 Gy is critical



Re-irradiation with IMRT

Author	n	Median FU	3-year survival	5-year survival	Stage I/II	Stage II/IV	Percentage receiving Chemo
Lu, 2004	49	0.75	100% control at 0.75 years	-	27%	73%	6%
Chua, 2005	31	0.92	30-40% at 2 years	-	26%	74%	68%
Koutcher, 2009	29	3.75	71%	60%	52%	48%	93%

Stereotactic Radiosurgery (SRS) Fractionated Stereotactic RT (FSRT)

Author	n	Modality	Median FU	3-year survival	5-year survival	Stage I/II	Stage III/IV
Pai, 2002	36	SRS	1.8	54%	31%	64%	36%
Shin, 2004	21	FSRT	4.1	-	32%	48%	52%
Low, 2006	25	SRS/BT	4.2	-	53%	100%	0%
Wu, 2007	56	FSRT	3.3	46%	-	68%	32%
Chua, 2007	74	SRS/BT	3.5	66-78%	-	70%	30%
Leung, 2009	30	SRS	-	65-67%	40%	70%	30%

New modalities that may make a difference

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Nasopharyngectomy: Radiation-sparring surgery?

- Ideal for rT1, rT2a and selected rT2b, rT3 cases
- Aim to achieve clear margins and spare re-RT
- May not improve survival
- Hopefully improves QOL

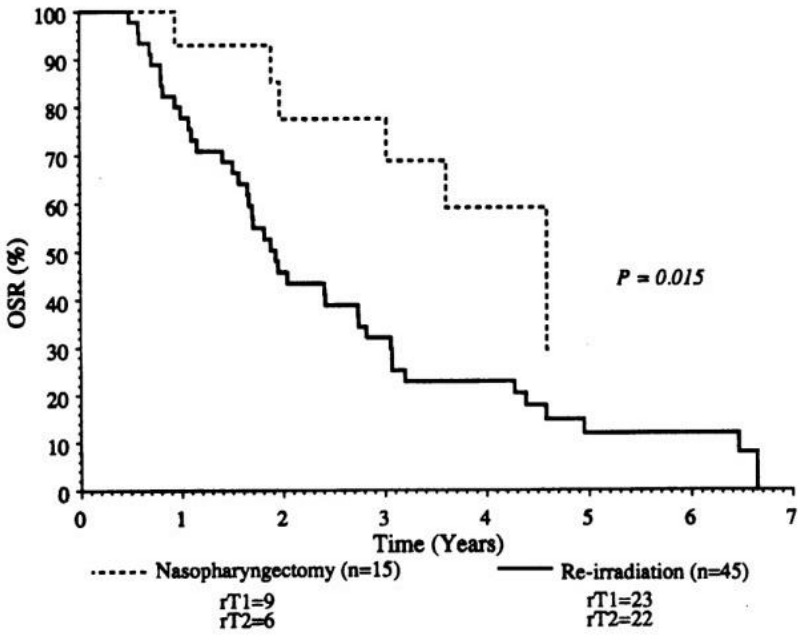
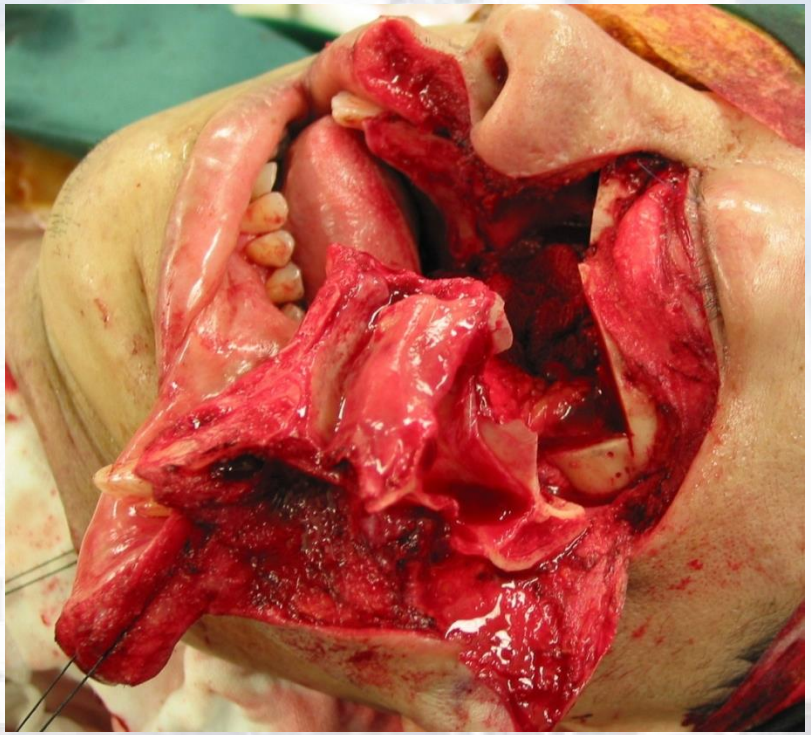


Fig. 11. Comparison of survival (OSR) between nasopharyngectomy and high-dose reirradiation for the rT1 and rT2.

Source: How successful is high-dose (> 60 Gy) reirradiation using mainly external beams in salvaging local failures of nasopharyngeal carcinoma? Teo PM et. al. (1998) Int J Radiat Oncol Biol Phys

Conventional approaches can incur significant morbidity

- For radical resection
  - Maxillary swing
  - Transpalatal-transmandibular
  - Mid-facial degloving
  - Lateral approach
- Maxillary swing approach gives better survival for early stage recurrence



Source: Nasopharyngectomy: Does the approach to the nasopharynx influence survival? Vlantis AC et. al. (2008) Otolaryngology – Head and Neck Surgery

Complications are common

- Fee's series of 37 cases had complication rate of 54%
- In King's series, the following complications were noted
  - Soft palate dysfunction (54.8%)
  - Trismus (48.4%)
  - Dysphagia (38.7%)
  - Nasal regurgitation (25.8%)

Source: Nasopharyngectomy for recurrent NPC a 2-17 year follow-up. Fee WE et. al. (2002)
Nasopharyngectomy in the treatment of recurrent NPC: a 12 year experience. King WW (2000)

Endoscopic Nasopharyngectomy

n = 37 patients

Recurrent T stage	Number
rT1	17
rT2a	4
rT2b	14
rT3	2

30/37 Previous RT

7/37 RT X 2

En bloc resection with negative margin in 35/37

195 minutes, 115 mls blood loss

None had further RT

Survival at 2 years	Percentage
Overall	84.2%
Local relapse-free	86.3%
Progression-free	82.6%

Source: Endoscopic Nasopharyngectomy for Locally Recurrent Nasopharyngeal Carcinoma. Chen M-Y et. al. (2009) Laryngoscope

Transoral robotic nasopharyngectomy?

- For larger tumours recurrences
- No clinical studies
- Cadaveric dissections show that it is feasible

Source: Transoral Robotic Nasopharyngectomy: A Novel Approach for Nasopharyngeal Lesions. Ozer E & Waltonen J (2008). Laryngoscope

Summary

- Early detection is probably the most important factor in managing recurrences
- Oncologically sound minimally invasive surgery will spare early recurrences re-irradiation
- New RT modalities should aim to improve QOL