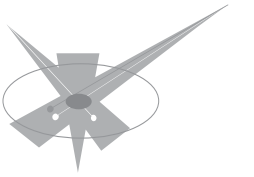
Rep Pract Oncol Radiother, 2005; 10(4): 193-201



Original Paper

Received: 2004.11.23
Accepted: 2005.06.15
Published: 2005.09.20

An analysis of outcomes, after re-irradiation by HDR (high-dose-rate) brachytherapy, among patients with locally recurrent nasopharyngeal carcinoma (NPC)

Joanna Terlikiewicz[1,2], Roman Makarewicz[1,2], Andrzej Lebioda[1,2], Renata Kabacińska[2,3], Marta Biedka[2]

[1] Brachytherapy Department, Oncology Centre, Bydgoszcz, Poland
[2] Oncology Department and Salvage Oncology Research Unit, Collegium Medicum, Mikołaj Kopernik University, Toruń, Poland
[3] Medical Physics Research Unit, Oncology Centre, Bydgoszcz, Poland

The proceedings from the 3rd Congress of the Polish Society of Radiation Oncology. Technical, Biological, and Clinical advance in radiotherapy, 13–16 October 2004, Bydgoszcz.

Summary

Background Despite aggressive treatment with radiotherapy, which is often combined with chemotherapy, local persistence occurs in 18–40% of patients with nasopharyngeal carcinoma. Brachytherapy is one of the methods for the re-treatment of patients with locally recurrent nasopharyngeal carcinoma.

Aim The aim of this paper was to evaluate the effectiveness of HDR (high-dose-rate) treatment of patients with locally recurrent nasopharyngeal carcinoma.

Materials/Methods The study took the form of a retrospective analysis and included a group of 28 patients treated in the Brachytherapy Department of the Oncology Centre in Bydgoszcz during the years 1995–2000. Brachytherapy was carried out using a Rotterdam applicator and the MicroSelectron HDR apparatus produced by Nucletron. Irradiation was based on doses of 36 Gy, i.e. 6 Gy applied once a week, and 51 Gy i.e. 3 Gy applied twice a week. This paper presents recovery probability, overall survival and recurrence-free survival within the analysed group of patients.

Results The results obtained prove intracavitary HDR (high-dose-rate) brachytherapy to be a viable method for the treatment of patients with recurring nasopharyngeal carcinoma.

Conclusions The higher the total dose applied by means of brachytherapy, the greater the chance of locally successful treatment, moreover, the time that elapses before recurrence is considered to be an important factor influencing recurrence-free survival time.

Key words **nasopharyngeal carcinoma • locally recurrent carcinoma • HDR (high-dose-rate) brachytherapy • re-irradiation, radiotherapy**

Full-text PDF: http:/www.rpor.pl/pdf.php?MAN=7836

Word count: 2755
Tables: 4
Figures: 9
References: 32

Author's address: Joanna Terlikiewicz, Brachytherapy Department, Oncology Centre, Romanowskiej 2 Str., 85-796 Bydgoszcz, Poland, e-mail: terlikiewiczj@co.bydgoszcz.pl

Background

Teleradiotherapy is a standard method for the treatment of patients with nasopharyngeal carcinoma. Unfortunately, despite aggressive irradiation, which is often combined with chemotherapy, local recurrence remains a major source of treatment failures, occurring in 18-40% of patients. Recurrence is classified as the development of a local tumour, usually occurring within a period of up to two years from completion of treatment [1–3].

Treatment of patients with recurrent nasopharyngeal carcinoma is a major challenge. Therapy includes numerous treatment options such as surgery, stereotactic radiosurgery, conventional radiotherapy, IMRT and brachytherapy [4–10]. Re-irradiating patients with recurrent nasopharyngeal carcinoma allows attainment of 25–52% rates of 3-year overall survival [6,11]. Achieving a complete recovery however, often results in post-irradiation complications. Therefore, reducing the irradiation of healthy tissues is absolutely vital and it is brachytherapy that provides us with an opportunity to do so. Use of this therapy facilitates the application of a high dose of radiation within a tumour while reducing it dramatically outside the treated field. Brachytherapy may be used either as an independent method of treatment or in association with external irradiation [4,5] for carefully selected groups of patients with local recurrent carcinoma, treated with radical teleradiotherapy.

Aim

The aim of this paper was to evaluate the effectiveness of HDR (high-dose-rate) treatment of patients with locally recurrent nasopharyngeal carcinoma.

Materials and Methods

A retrospective analysis of a group of 28 patients with recurring nasopharyngeal carcinoma was carried out. The patients were treated between 1995 and 2000 in the Brachytherapy Department of the Oncology Centre in Bydgoszcz. Detailed characteristics of the patients are shown in Table 1. Local recurrence was defined as the presence of a tumour shoot 6 months or more after complete regression, following completion of the treatment. The observation period in all cases was at least 12 months. After histopathological verification of recurrence, each patient underwent a series of other tests. These tests included: an ENT check-up, computerized tomography, a chest x-ray, an endoscopic examination, and an ultrasound scan of the abdominal cavity and neck. The patients were classified as suitable for brachytherapy provided that they met the following conditions: the tumour had to be restricted to the upper larynx and must have measured 15 millimetres or less, there must have been no metastases to the lymph glands, nor should any remote metastases have been observed, local recurrence must have been histopathologically verified at least 6 months after total regression of a tumour following teleradiotherapy treatment. Having locally anaesthetized the mucous membrane, a Rotterdam applicator was introduced into the nasopharynx. Radiological images were made in the antero-posterior and lateral planes (Figures 1,2). These images constituted the basis for calculating doses for both the tumour and for the healthy tissues (Figure 3). Tumour dose was calculated at the so called "nasopharyngeal point" (Na), which is situated at the intersection of a line joining the soft palate reference point and the point of the skull base bone. The distance between the Na point and the axis ranged from 0.75 to 1 cm depending on the position of the applicator, which, in turn, depended on individual patients' anatomy. In case of a suboptimal layout of doses throughout the reference points, optimisation took place. After a plan had been completed and accepted by a doctor, catheters were introduced into an applicator (R/Silisonide aerosol was used to facilitate their introduction) and then connected, by means of transferring cables, to the MicroSelectron HDR apparatus produced by Nucletron (Ir 192) (Figure 4). The patient remained in contact with the doctor carrying out the treatment (being able to hear and see the doctor) throughout the procedure, which usually did not exceed a few minutes. The applicator was removed from the nasopharynx following the completion of the whole course of treatment. Whenever necessary, analgesic substances, steroids and irrigation were used in order to improve treatment tolerance.

Irradiation involved total doses of 36 Gy, i.e. 6 Gy applied weekly, (until 1999, in 18/28 (64.3%) of the patients) and 51 Gy, i.e. 3 Gy, applied twice daily, (after 1999 in 10/28 (35.7%) of the patients).

A normalized total dose (NTD_2) was calculated by means of the following formula:

$$NTD_2 = D_{total} * (df + \alpha\langle/\beta) / (2 + \alpha/\beta),$$

Table 1. Clinical characteristics of patients with recurrence of nasopharyngeal cancer.

Gender	
Male	17 (60.7%)
Female	11 (39.3%)
Age	
Average	18–73 [57,9]
Male	59.9
Female	54.4
Histology	
Lymphoepithelioma	20 (71.4%)
Other	8 (28.6%)
Pre-treatment T-stage	
T_1	0
T_2	9 (32.1%)
T_3	9 (32.1%)
T_4	6 (21.4%)
T_x	4 (14.4%)
Pre-treatment N-stage	
N_0	9 (32.1%)
N_1	11 (39.3%)
N_2	7 (25%)
N_3	1 (3.6%)
Total dose received (external beam radiotherapy)	
Average	66–74

where:
D_{total} – total dose
D – fractionated dose

The value of α/β 10 Gy was accepted.

Statistical analysis was carried out by means of the program Statistica for Windows and using the Kaplan-Meier method, the log rank test, a multifactor Cox analysis and logistic regression models.

Results

Evaluation of treatment response was carried out on the basis of ENT, endoscopic examinations and, in some cases, by means of computerized tomography. 6 weeks after treatment completion, CR, PR and NC responses were noted in 64.5% (18/28), 32% (9/28) and 3.5% (1/28) of cases respectively. The median overall failure-free survival period for the whole group was 76 months. The probabilities of surviving 3 or 5 years were 67% and 60% respectively (Figure 5). Nevertheless, an analysis of median overall failure-free survival time within the group of patients diagnosed with poorly differentiated nasopharyngeal carcinoma (WHO 3) showed 3 and 5 year survival rates of 60% and 55% respectively, and among other patients 80% and 70% respectively. No statistically significant differences in survival rates were noted for the compared groups (72 vs. 77 months, log rank test p=0.98) (Figure 6).

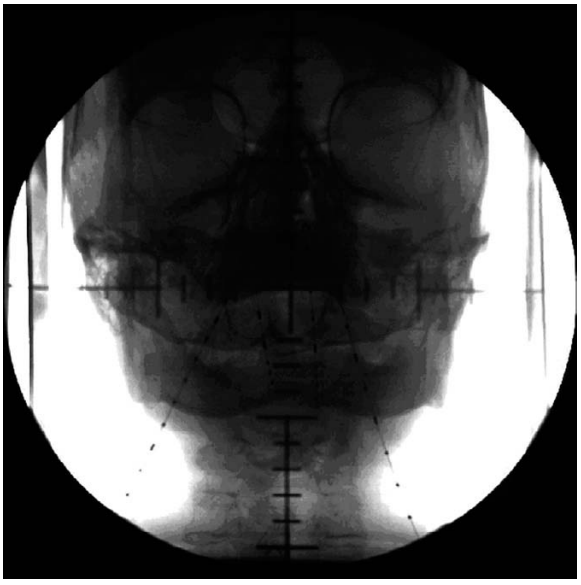


Figure 1. Radiological demonstration of a Rotterdam applicator – A-P projection.

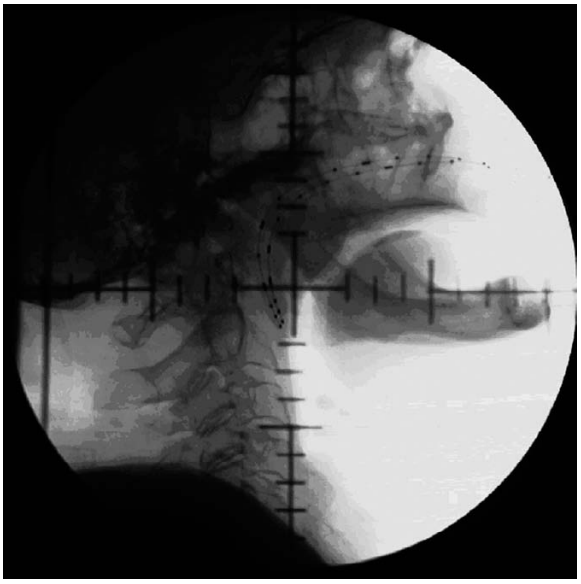


Figure 2. Radiological demonstration of a Rotterdam applicator – lateral projection.

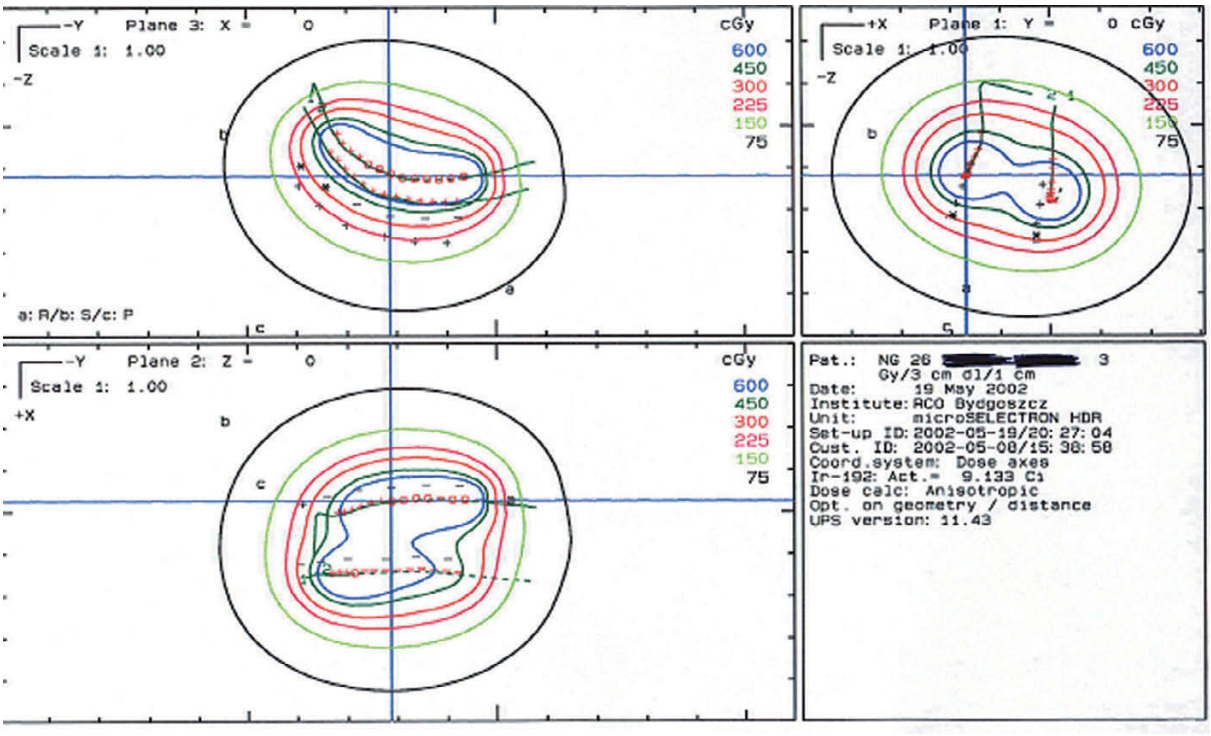


Figure 3. Isodose distribution generated from HDR brachytherapy in patients with recurrence of nasopharyngeal cancer.

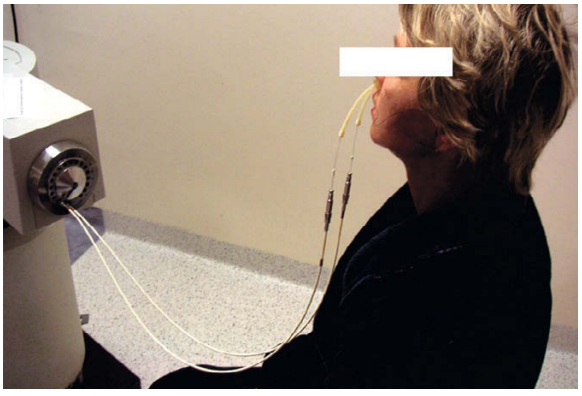


Figure 4. A patient during a course of brachytherapy.

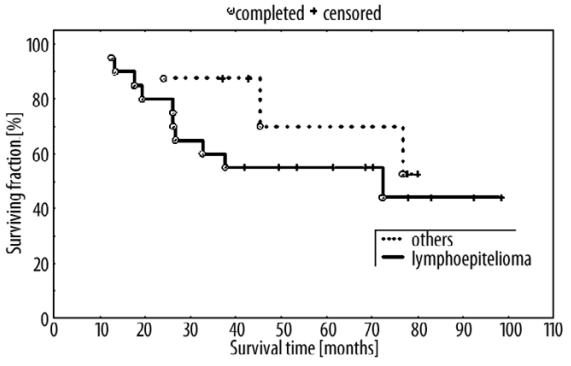


Figure 6. A comparison of overall survival time with histopathological diagnosis (p=0.98).

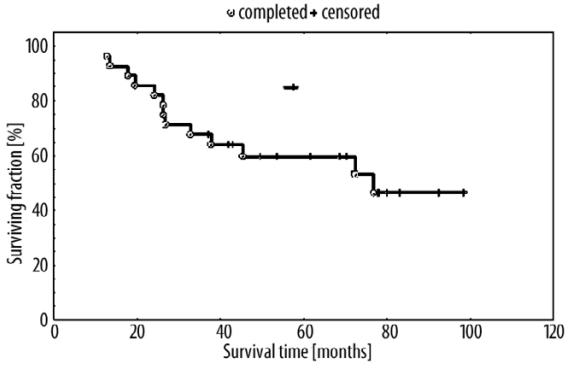


Figure 5. Overall survival time in patients after secondary radiotherapy.

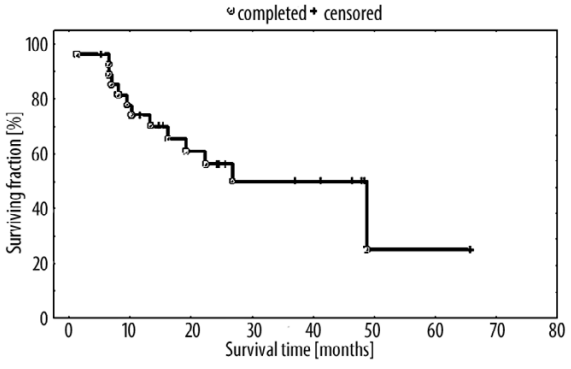


Figure 7. Overall recurrence free survival time after secondary radiotherapy.

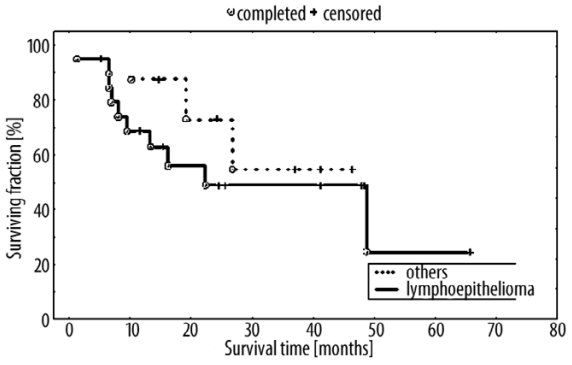


Figure 8. A comparison of recurrence-free survival time with histopathological diagnosis (p=0.88).

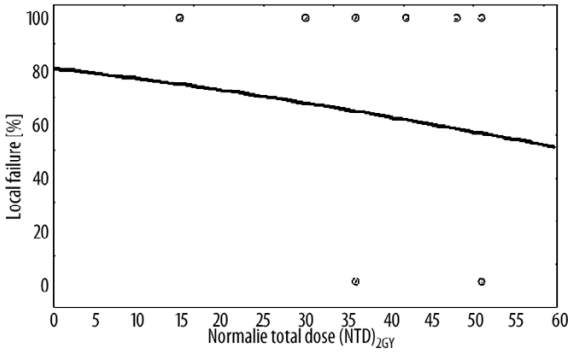


Figure 9. The risk failure, relative to biological dose.

Table 2. The influence of selected factors on overall survival time in patients with recurrence of nasopharyngeal cancer: multivariate Cox analysis.

Factor	p
Age	0.03
Pre-treatment T-stage	0.01
Total dose received (external beam radiotherapy)	0.03
Total dose received (brachytherapy)	0.4

Table 3. The influence of selected factors on overall recurrence free survival time in patients with nasopharyngeal cancer: multivariate Cox analysis.

Factor	p
Pre-treatment T-stage	0.1
Pre-treatment N-stage	0.9
Total dose received (brachytherapy)	0.3
Fractional dose received (brachytherapy)	0.3
Total dose received (external beam radiotherapy)	0.8
Time to progression	0.01

Median overall recurrence-free survival time was 26 months for the whole group. The probabilities for 3 and 5 year recurrence-free survival rates for the whole group were 50% and 25% respectively (Figure 7).

The survival rates for 3 and 5 recurrence-free years within the group of patients diagnosed with poorly differentiated nasopharyngeal carcinoma (WHO 3) were 48% and 24% respectively, while within the group of patients with other histopathological diagnoses, the survival rate for 3 years was 55%. An analysis of median recurrence-free survival times, depending on histopathological diagnosis, showed no differences between groups (log rank test p=0,88) (Figure 8). A multi factor Cox analysis showed age, T feature, total dose applied during teleradiotherapy and total dose applied during brachytherapy to be statistically significant influences on overall survival time. However, these factors were not considered to influence recurrence-free time. According to the Cox analysis, the only factor significantly influencing the time span for local recurrence-free survival was the time elapsed before local recurrence actually developed (Tables 2,3).

The higher the normalized total dose, applied by means of brachytherapy, the larger the increase in chances for local recovery (Figure 9).

During and immediately after treatment, all patients developed acute radiation induced reactions in the form of inflamed mucous membranes of the upper larynx. No patients developed retarded radiation induced complications. No data was recorded in this respect in the cases of 15 patients.

Discussion

18–24% of patients with nasopharyngeal carcinoma develop local recurrences despite increasingly advanced technology in treatment methods [4,11]. Academic literature lacks universally accepted rules for the definition of local recurrence and for calculating the time available for

the implementation of salvage treatment. Most authors define local recurrence based on the time in which it is developed, which ranges from 3 to 4–6 months from the first teleradiotherapy [12–15]. Some authors define recurrence as a tumour shoot following complete regression and disregard the time of its occurrence, while others fail to give any explicit definition of recurrence [5,16,17]. Throughout this paper, a cut-off period of 6 months is assumed to allow local recurrence to be set apart from tumours that have not been successfully treated. Division into early and late recurrences is clear-cut. Late recurrences are normally defined as being those that develop at least 2 years after the first radiotherapy and in such cases it is easier to make a decision as to whether or not to implement salvage treatment than in cases of early recurrence [5,18].

It is difficult to classify a patient with recurrent nasopharyngeal carcinoma, who has just undergone radical teleradiotherapy, with regard to proper treatment. According to most publications re-irradiation allows attainment of 5 year survivals in 20–40% of all cases, while treatment employing external radiation beams, even when treating relatively small tumours (T1-2) may result in severe late complications [15,19]. Poor results from teleradiotherapy and high mortality rates in surgical treatment make brachytherapy appear to be a good alternative, especially for patients with early advanced local recurrence (rT1, rT2), as is the case in about 35% of all patients developing recurrence.

Our centre used re-irradiation by means of independent brachytherapy in the cases of 28 patients with recurrent nasopharyngeal carcinoma. The academic literature features papers analysing extremely varied groups of patients. Analyses included both patients with recurrent upper larynx carcinoma, at different developmental stages, and patients with local treatment failures. The groups were often merged in analyses. It must be categorically stated that, as a basic condition, no patients with remote metastases were accepted for re-irradiation. Table 4 includes examples of total doses and patient groups that underwent analysis.

Our centre uses an Irydium192 source, an HDR afterloading technique, and total doses ranging from 36 to 51 Gy to irradiate patients with recurrent nasopharyngeal carcinoma. Other authors have described using similar techniques and doses [16,20].

Syed and co-workers presented an interesting combination of intratissue and intracavitary techniques in treating patients, including those with recurrent nasopharyngeal carcinoma. They employed a manual afterloading technique and Ir sources whose average activities were 84 mCi. Doses averaged 46.7 Gy and the treatment time span was 105.9 hours [22].

Similar techniques and doses have been used to patients with recurring nasopharyngeal carcinoma in Japan (total doses 50–58 Gy, manual afterloading, intratissue and intracavitary technique, Ir and Au sources) [12,23].

Lee et al. analysed treatment results within a group of 576 patients with nasopharyngeal carcinoma treated between 1995 and 2000. The patients underwent brachytherapy so as to increase the doses following teleradiotherapy, both in treating the primary tumours and the recurrences. 55 patients from this group underwent brachytherapy as treatment for both the primary and the recurrence. Numerous applicators were used, including Rotterdam, balloon, and ovoid types and there were various strong doses – LDR, HDR, and PDR. Within the group of patients with recurrent nasopharyngeal carcinoma, 64.5% of patients enjoyed total tumour regression, while 32% enjoyed partial regression. On the basis of their analysis, the authors concluded that increasing brachytherapy dose is an effective and well-tolerated method for the treatment of both primary tumours and recurrent nasopharyngeal tumours [24].

Law et al. presented a paper describing the mould technique and irradiation by means of iridium rods used only in cases of patients with recurrent nasopharyngeal carcinoma. Total regression was noted in 97% of all cases while 5-year locally successful treatments, recurrence free survival rates and average survival rates amounted to 85%, 68.3% and 61.3% respectively [23].

Sham et al. reported lower locally successful treatment rates (28%), having treated 30 patients with recurrent and persistent nasopharyngeal tumours by means of intracavitary techniques using caesium sources and intratissue techniques employing gold sources [25].

Kwong et al. reported brachytherapy to be an effective salvage treatment in cases of selected groups of patients with either primary or recurrent carcinoma restricted to the nasal por-

Table 4. Results of radiotherapy in patients with recurrence of nasopharyngeal cancer.

Study	Treatment	Number of patients	Recurrence T-stage	5-years regional control (%)	5-years free survival from recurrence (%)	5-years survival (%)	Complications (category, frequency)
Pryzant [19]	EBR+BTH BTH	53	1–2	35	18	21	CNS complications – 15%
Theo [28]	BTH 24 Gy/3 fr	71	1–4	69	58	–	The gentle tissue necrosis – 7%
Zhang [29]	EBR (45–65 Gy) + BTH (20–50 Gy	29	1–2	–	–	55.5 (after 4 years)	Trismus – 100%
Wang [30]	EBR (40–66 Gy) + BTH (20 Gy)	51	1–4	–	–	T1-2 – 38 T3-4 – 15	–
Yang [31]	EBR (50 Gy) + BTH + CHTH	77	–	–	–	17–36 (after 2 years)	–
Leung [16]	EBR (44 Gy + BRTH (24–36 Gy)	61	–	45–82% (3 years)	–	62–82 (after 3 years)	Trismus – 18%
Lee [32]	EBR (40–57 Gy + BRTH (10–20 Gy)	706	1–4	23	–	14	–
Choy [33]	BTH	43	–	44–81	–	25–65	Tissue necrosis-fistula 16%
Syed [22]	BTH 50–58 Gy	41	1–4	59	41	30	Tissue necrosis, dysphagia, 11–14%

EBR – External Beam Radiotherapy; BTH – brachytherapy; CHTH – chemotherapy.

tion of the larynx. Making use of gold sources and the intratissue technique, the authors analysed 3 groups of patients and obtained the following 5 year locally successful treatment rates: 87% within a group with persistent tumours, 62% within a group with a first local recurrence and 23% within a group with a second local recurrence (p.=0.0004). Average 5-year survivals within those groups were 79.1%, 60.1% and 42.9% (p.=0.0047) respectively [21].

Overall 5-year survival rates for the group treated in our centre was 60%, which was similar to results reported by other authors [20,23].

Fisher and Partners report lower overall 5-year survival rate (46%) within their group of 13 patients [26].

Our own research allowed us to estimate the probability of a 5-year disease-free survival at 25%.

Syed and Partners reported higher local recurrence-free survival rates (59%) within the group of patients with recurrent and unsuccessfully treated nasopharyngeal carcinoma [22]. Within the group that we treated the there were no differences between the probability of the overall survival time and the probability of recurrence-free survival time as far as the two groups with different histopathological check-up results were concerned. No similar analysis has been found in academic literature.

Leung and Partners show irradiation results within the group of 87 patients with unsuccessfully treated nasopharyngeal carcinoma, who, irrespectively of the tumour range, were treated by means of the HDR afterloading technique employing Co^{60} or Ir^{192} sources (total doses ranged from 22.5 to 25 Gy within 3 week following teleradioteraphy). Treatment results in case of those patients were compared with results within the group of 3393 patients undergoing teleradiotheraphy. 5-year recurrence-free survival rates within these groups were respectively 85% and 76.6% [17].

The multifactor Cox analysis proved materials we have researched to include statistically significant influences on the overall survival time: age, T features, total dose applied during teleradiotherapy and total dose applied during brachytherapy.

Neither of these factors has been noted to influence recurrence-free survival time. According to the multifactor Cox analysis, the only significant influence on recurrence-free survival time, was the time elapsed to developing a local recurrence. Age influence on the average survival time and the disease-free survival time shown in the multifactor Cox analysis has been confirmed by papers of other authors [17,21,22].

The paper presented by Syed and Partners analyses influences of sex, age, tumour range and lymph gland state on disease-free survival time. Probabilities of 2-, 5-, and 10- year survivals reached respectively 48%, 30% and 20%, while 2-, 5-, and 10- locally successful treatment reached respectively 81%, 59%, 49%, and 2-, 5-, 10- year disease-free survival time was respectively 56% 41% 34% [22].

Leung and Partners state that T feature was the only factor in the Cox analysis found to be significant for assessing influences that different parameters exert on chances of locally successful treatment. Other parameters, such as age, sex, persistent tumours or use of brachytherapy had no influence on treatment results. The authors concluded that persistent nasopharyngeal carcinoma may be successfully treated by means of brachytherapy and that patients within the early stages of carcinoma development enjoy better results. Their analysis proved the T feature to be a more significant factor than obtaining a clinical remission after teleradiotherapy [17]. A multifactor analysis, presented in a paper by Kwung and co-workers, states that the reason for classifying a patient into a certain type of treatment group (based on persistent disease, first or second recurrence) was the only factor significantly influencing survival rates [12].

Chua et al. observed 34 patients with recurrent nasopharyngeal carcinoma who were diagnosed by computerized tomography and treated with brachytherapy. Their observations showed that patients with shorter recurrence-free time spans enjoyed longer survivals than those with longer disease-free periods. As the authors explain, this effect was caused by the fact that patients with early recurrence often have relatively small tumour volumes in comparison to cases of late recurrence [14].

Early post radiation reactions of low intensity occurred in all cases in the group we treated. Other authors have reported similar data [16,22,25,27,28].

Late complications resulting from re-irradiating patients with nasopharyngeal carcinoma include: soft palate necrosis, temporal lobe necrosis (12%), deteriorated eyesight (9%), deteriorated hearing (13%), jaw clenching (30%) and endocrine disorders (10%). These complications occurred more frequently in patients whose treatment combined brachytherapy with teleradiotherapy, in order to cure local recurrences [22,27,29–32].

Our material featured no late complications. However, it must be noted that some of the patients did not undergo any detailed observation in this respect and late complications might still ensue.

Conclusions

1. HDR intracavitary brachytherapy is an effective treatment method in cases of patients with recurrent nasopharyngeal carcinoma.

2. The period elapsed before development of local recurrence is a significant factor influencing disease-free survival times.

3. The chances for successful local treatment among patients with nasopharyngeal carcinoma improves with increased total dose applied during brachytherapy.

References:

1. Lavendag T, Schmitz PI, Jansen PP et al: Fractionated high-dose-rate brachytherapy in primary carcinoma of the nasopharynx. J Clin Oncol, 1998; 16: 2213–20
2. Özyar E,F, Akyol FH: Comparison of AJCC and 1997 classifications for nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys, 1999; 44: 1079–88
3. Wang CC: Accelerated hyperfractionation radiation therapy for carcinoma of the nasopharynx techniques and results. Cancer, 1989; 63: 2461–7
4. Teo PM, Kwan WH, Chan AT et al: How successful is high-dose (>or=60 Gy) reirradiation using mainly external beams in salvaging local failures of nasopharyngeal carcinoma? Int J Radiat Oncol Biol Phys, 1998; 40: 897–913
5. Wang CC: Re-irradiation of recurrent nasopharyngeal carcinoma-treatment techniques and results. Int J Radiat Oncol Biol Phys, 1987; 13: 953–6

6. Lee AW, Law SC, Foo W et al: Retrospective analysis of patients with nasopharyngeal carcinoma treated during 1976–1985: Survival after local recurrence. Int J Radiat Oncol Biol Phys, 1993; 26: 773–82
7. Tu GY, Hu YH, Xu GZ et al: Salvage surgery for nasopharyngeal carcinoma. Arch Otolaryngol Head Neck Surg, 1998; 114: 328–9
8. Erickson BA, Wilson JF: Nasopharyngeal brachytherapy. Am J Clin Oncol, 1993; 16: 424–3
9. Chua DT, Sham JS, Hung KN et al: Stereotactic radiosurgery as a salvage treatment for locally persistent and recurrent nasopharyngeal carcinoma. Head Neck, 1999; 21: 620–6
10. Sultanem K, Shu HK, Xia P et al: Three-dimensional intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: The University of California-San Francisco experience. Int J Radiat Oncol Biol Phys, 2000; 48: 711–22
11. Lee AW, Law SC, Foo W et al: Nasopharyngeal carcinoma: Local control by megavoltage irradiation. Br J Radiol, 1993; 66: 528–36
12. KwongDL, Wei Wl, Cheng AC et al: Long term results of radioactive gold grain implantation for the treatment of persistent and recurrent nasopharyngeal carcinoma. Cancer, 2001; 91: 1105–13
13. Hwang JM, Fu KK, Phillips TL: Results and prognostic factors in the retreatment of locally recurrent nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys, 1998; 41: 1099–111
14. Chua DT, Sham JS, Hung KN et al: Salvage treatment for persistent and recurrent T1-2 nasopharyngeal carcinoma by stereotactic radiosurgery. Head Neck, 2001; 23: 791–8
15. Lee AW, Foo W, Law SC et al: Reirradiation for recurrent nasopharyngeal carcinoma: Factors affecting the therapeutic ratio and ways for improvement. Int J Radiat Oncol Biol Phys, 1997; 38: 43–52
16. Leung TW, Tung SY, Sze WK et al: Salvage brachytherapy for patients with locally persistent nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys, 2000; 47: 405–12
17. Leung TW, Tung SY, Sze WK et al: Salvage radiation therapy for locally recurrent nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys, 2000; 48: 1331–8
18. Lee AW, Foo W, Law SC et al: Recurrent nasopharyngeal carcinoma: The puzzles of long latency. Int J Radiat Oncol Biol Phys, 1999; 44: 149–56
19. Pryzant RM, Wendt CD, Delclos L et al: Re-treatment of nasopharyngeal carcinoma In 53 patients. Int J Radiat Oncol Biol Phys, 1992; 22: 941–7
20. Lengyel E, Baricza K, Somogyi A et al: Reirradiation of locally recurrent nasopharyngeal carcinoma. Strahlender Onkol, 2003; 179(5): 298–305
21. Kwong DL, Wei WI, Cheng AC et al: Long term results of radioactive gold grain implantation for the treatment of persistent and recurrent nasopharyngeal carcinoma. Cancer, 2001; 91(6): 1105–13
22. Nisar Syed AM et al: Brachytherapy for primary and recurrent nasopharyngeal carcinoma: 20 years' experience at long beach memorial. Int J Radiat Oncol Biol Phys, 2000; 47: 1311–21
23. Law SCK, Lam W-K, Ng M-F et al: Reirradiation of nasopharyngeal carcinoma with intracavitary mould brachytherapy: an effective means of local salvage. Int J Radiat Oncol Biol Phys, 2002; 54: 1095–113
24. Lee N, Hoffman R, Phillips TL et al: Managing nasopharyngeal carcinoma with intracavitary brachytherapy: one institution's 45-year experience. Brachytherapy, 2002; 1(2): 74–82
25. Sham JS, Wei WI, Choy D et al: Treatment of persistent and recurrent nasopharyngeal carcinoma brachytherapy. Br J Radiol, 1989; 62(736): 355–61
26. Fischer M, Stuben G, Stuschke M et al: Brachytherapy with (192)Iridium in the treatment of recurrent nasopharyngeal carcinoma. Laryngorhinootologie, 2002; 81(2): 106–10
27. Daniel TT, Chua FR, Jonathan CR Sham ST et al: Locally recurrent nasopharyngeal carcinoma: treatment results for patients with computed tomography assessment. Int J Radiat Oncol Biol Phys, 1998; 41: 379–86
28. Teo P, Leung SF, Choi P et al: Afterloading radiotherapy for local persistence of nasopharyngeal carcinoma. Br J Radiol, 1994; 67: 181–85
29. Zhang E-P, Lian P-G, Cai K-L et al: Radiation therapy of nasopharyngeal carcinoma: Prognostic factors based on a 10-year follow-up of 1302 patients. Int J Radiat Oncol Biol Phys, 1989; 16: 301–5
30. Wang CC: Improved local control of nasopharyngeal carcinoma after intracavitary brachytherapy boost. Am J Clin Oncol, 1991; 14: 5–8
31. Yang T-S, Ng K-T, Wang H-M et al: Prognostic factors of locoregionally recurrent nasopharyngeal carcinoma: A retrospective review of 182 cases. Am J Clin Oncol, 1996; 19: 337–43
32. Lee Anne WM, Law SCK, Foo W et al: Retrospective analysis of patients with nasopharyngeal carcinoma treated during 1976–1985: Survival after local recurrence. Int J Radiat Oncol Biol Phys, 1993; 26: 773–82