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FAST NEUTRON RADIOTHERAPY

The University of Washington experience

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An overview of the University of Washington neutron radiotherapy facility is presented. The utility of the multi-leaf, programmable, variable collimator is emphasized. Due to success in the treatment of salivary gland tumors, such patients comprise an ever increasing portion of the patients being treated. A cooperative randomized clinical trial for the treatment of salivary gland tumors was undertaken comparing fast neutrons against photon/electron radiation. At ten years, there was a statistically significant improvement in local/regional control for the neutron group (56% vs 25%, p = 0.009), but there was no improvement in survival (15% vs 25%, p = n.s.). Distant metastases were the primary reason for the failure of improved local/regional control to impact survival in the neutron group. The University of Washington experience is summarized with special emphasis on the treatment of adenoid cystic carcinomas. Excellent local/regional control can be achieved with neutrons even for large tumors arising in the paranasal sinuses. We conclude that the potential morbidity of a surgical debulking procedure is not warranted in most clinical situations.

Malignant salivary gland tumors are relatively rare, comprising about 1–3% of all head and neck malignancies (1). Treatment of inoperable salivary gland tumors with low linear energy transfer (LET) radiation, such as photons or electrons, has generally been of limited success. Overall local/regional control with low LET radiation using conventional fractionation schemes has averaged less than 30% (2–14). Accelerated hyperfractionated radiation using photons with or without electrons or interstitial boost (1.6 Gy per fraction b.i.d. to a total dose of 65–70 Gy) has resulted in a crude local/regional control of 75% (15). However, this was a small series of patients, and the study was not randomized. With the poor outcome using low LET radiation and the typically superficial location for inoperable salivary gland malignancies, these tumors represented a logical site for testing in early neutron trials using the poorly penetrating beams which were initially available.

There have been numerous non-randomized series of patients with malignant salivary gland tumors which have been reported in the literature following treatment with conventionally fractionated irradiation (2–14, 16–24). Tables 1 and 2 provide a comparison of these studies for patients with inoperable or recurrent salivary gland tumors treated with low LET and neutron radiotherapy respectively. A general trend toward improved local/regional control is observed with neutron radiation compared to low LET radiation. This trend is consistent with data which suggest a relative biological effectiveness for neutrons of 8.0 in adenoid cystic carcinoma (25).

The reported series summarized in Tables 1 and 2 typically consist of small numbers of patients, multiple histologies, and a spectrum of follow-up intervals. Furthermore, the earlier studies, for both low LET and neutron radiation, were undertaken with equipment and treatment planning systems which were less sophisticated than those

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Table 1

Local/regional tumor control rates for malignant salivary gland tumors using low LET (photon/electron) radiotherapy in conventional fractionation schemas from nonrandomized studies

	Patient No.	Control rate
Fitzpatrick & Thoriault (2)	50	12% (6/50)
Vikram et al. (3)	49	4% (2/49)
Borthne et al. (4)	35	23% (8/35)
Rafla (5)	25	36% (9/25)
Fu et al. (6)	19	32% (6/19)
Stewart et al. (7)	19	47% (9/19)
Ellis et al. (8)	17	29% (5/17)
Dobrowsky et al. (9)	17	41% (7/17)
Shidnia et al. (10)	16	38% (6/16)
Guillamondi et al. (11)	15	60% (9/15)
Elkon et al. (12)	13	15% (2/13)
Ravasz et al. (13)	12	25% (3/12)
Rossman (14)	11	54% (6/11)
Total	298	26% (78/298)

Table 2

Local/regional tumor control rates for malignant salivary gland tumors using high LET fast neutron radiotherapy from nonrandomized studies

	Patient No.	Control rate
Saroja et al. (16)	113	63% (71/113)
Catterall & Errington (17)	65	77% (50/65)
Buchholz et al. (18)	52	77% (40/52)
Batterman & Mijnheer (19)	32	66% (21/32)
Duncan et al. (20)	22	55% (12/22)
Maor et al. (21)	9	67% (3/8)
Ornitz et al. (22)	8	38% ((3/8)
Eichhorn et al. (23)	5	60% (3/5)
Skolyszewski et al. (24)	3	67% (2/3)
Total	309	67% (208/309)

which are available today. In light of these conditions, a randomized prospective trial was undertaken by the Radiation Therapy Oncology Group (RTOG) in the United States and the Medical Research Council (MRC) in Great Britain to compare neutron versus photon radiation in the treatment of unresectable salivary gland malignancies. We will present here an overview of the RTOG/MRC randomized trial and the impact of modern high energy neutron facilities on the delivery of this mode of radiation, using the University of Washington unit as an example.

RTOG/MRC randomized trial

Thirty-two patients were entered on the RTOG/MRC randomized trial for treatment of unresectable salivary gland malignancies from July of 1980 through March of 1986. Results have been reported with follow-up out to 2 and 10 years (26, 27). The schema for this study is shown

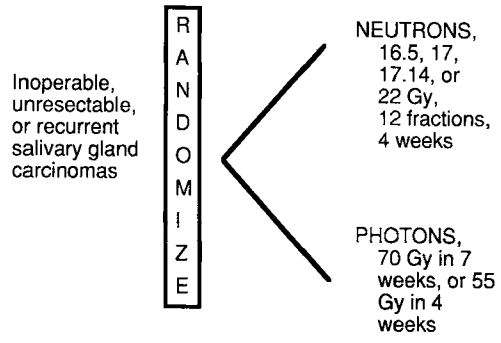

Fig. 1. Randomization scheme for inoperable and unresectable primary and recurrent salivary gland tumors. The neutron dose is adjusted for the institutional neutron scaling factors.

in Fig. 1. To be eligible for this study, patients had to have either inoperable or unresectable primary or recurrent malignant tumors of the major or minor salivary glands. Patients with unmeasurable postoperative residual disease were ineligible. The eligible histologies were mucoepidermoid carcinoma, acinic cell carcinoma, adenoid cystic carcinoma, adenocarcinoma, squamous cell carcinoma, and malignant mixed tumors. Other eligibility requirements were patient age between 18 and 76 years, no history of other prior malignancies (other than non-melanoma skin cancer), no prior radiation therapy, and a Karnofsky performance status of at least 60. Patients were randomized to receive either fast neutron radiation or conventional megavoltage radiation with photons and/or electrons.

For the low LET arm, patients from the United States received 70 Gy delivered over 7.5 weeks, and patients from Scotland received 55 Gy delivered over 4 weeks, reflecting treatment conventions within each country which were felt to be clinically equivalent. For the neutron arm, radiation, was delivered with 12 fractions, 3 fractions per week, over 4 weeks. The planned neutron dose varied slightly between the four participating facilities, based upon radiobiological intercomparison studies (27). Thirty-two patients were entered on this study, and 25 were eligible and evaluable (12 on the photon arm and 13 on the neutron arm). Lymph nodes were involved in 33% of the photon patients and 54% of the neutron patients. Twenty-five percent of the photon patients and 39% of the neutron patients were entered on the study with recurrent disease (27).

The 2-year analysis (27) showed dramatic improvement with neutrons over photons with respect to local/regional control (67% for neutrons versus 17% for photons, $p < 0.005$) and local/regional complete response (85% for neutrons versus 33% for photons, $p = 0.01$). A trend toward improved 2-year survival was evident ($p = 0.1$) for neutrons (62%) compared to photons (17%). Although only 32 patients had been entered onto this study, with only 25 being eligible and evaluable, the participating neutron facilities became reluctant to continue this study

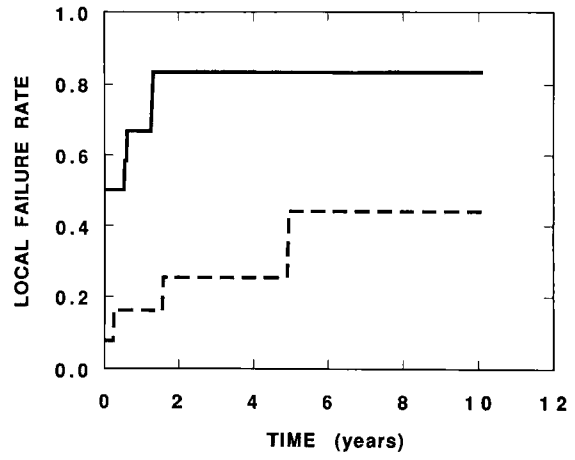

Fig. 2. Probability of local/regional failure for patients entered on the two treatment arms of the protocol. Photon arm: ——; neutron arm – – –. The starting values of the curves represent the initial local/regional failure rates. The difference between the two curves is statistically significant at the $p = 0.009$ level.

in light of the impressive differences at two years. For this reason, the study was closed early for ethical reasons (26).

The most recent analysis of this study includes data up to 10 years with a minimum 'time-at-risk' of 6 years (26). Actuarial local/regional failure out to 10 years for the neutron and low LET arms is shown in Fig. 2. The crude incidence of failure has been 75% for the photon arm and 31% for the neutron arm. The 10-year actuarial local/regional control probability was 17% for the photon arm and 56% for the neutron arm ($p = 0.009$). Survival data expressed on an actuarial basis are shown in Fig. 3. The crude survival has been 25% and 23% for the photon and neutron arms respectively. The 10-year actuarial survival was 25% for the photon patients versus 15% for the neutron patients, with no statistically significant difference between the two curves ($p = 0.5$).

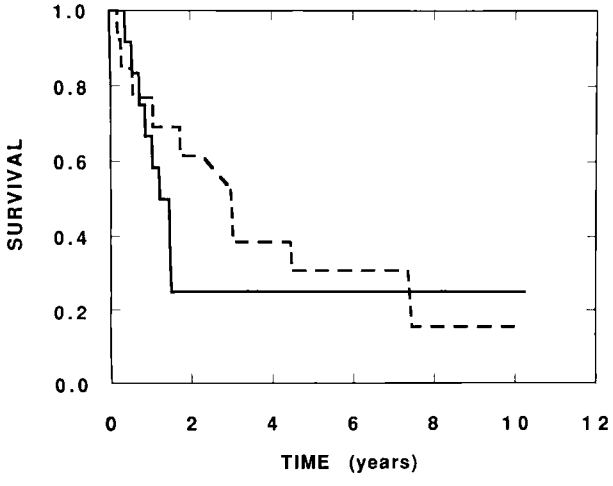

Fig. 3. Survival probabilities for the patients on the two treatment arms of the protocol. Photon arm: ——; neutron arm; – – –. There is no statistically significant difference between the two curves ($p = 0.50$).

Although the superiority of neutron radiotherapy in the control of unresectable malignant salivary gland tumors has held up over time, the early trend toward improved survival has not. This may be attributable to the development of metastatic disease. Distant metastases occurred in 7 patients on the photon arm (4 of which were associated with local/regional failure) and in 9 patients on the neutron arm (4 of which were associated with local/regional failure). The longer median survival of the neutron group (36 months versus 15 months) suggests that improved local/regional control may have allowed for clinical manifestation of pre-existing subclinical metastatic disease in patients who otherwise would have succumbed to local/regional disease (26).

Morbidity of any degree involving any system was experienced by 10 of the patients treated with photons and by all 13 patients treated with neutrons. 'Severe or greater' complications, as defined by the joint RTOG/EORTC scoring system, occurred in 4 of the patients on the photon arm and 9 of the patients on the neutron arm ($p = 0.07$). 'Life-threatening' complications occurred in one photon patient and in 2 neutron patients. There were no deaths referable to radiation on either arm. Although the morbidity associated with neutron radiotherapy appeared somewhat greater than that with low LET radiation, it did not disrupt treatment delivery in such a way as to impact local/regional control (26).

The conclusions from this study were that fast neutron radiotherapy is the 'treament-of-choice' for patients with unresectable salivary gland malignancies, morbidity from neutron therapy is acceptable, and distant metastasis remains a substantial detriment to survival even with improved local/regional control (26).

Impact of modern high energy neutron facilities on treatement delivery

Development of hospital-based neutron treatment facilities

In 1971, the National Cancer Institute (NCI) approved a program project grant for the University of Washington to modify a physics laboratory-based cyclotron for clinical use (28). These laboratory-based units had severe limitations in terms of treatment delivery: beams could be delivered only from a horizontal axis a fixed distance from the floor, dose distributions were limited by low beam energy with poor depth dose characteristics and poor skin sparing, beam collimation was inadequate, and there were limitations to machine availability for clinical use. Phase I and II trials demonstrated excessive normal tissue toxicity associated with treatment of deeply located tumors due to poor dose distribution. Consequently, early phase III trials consisted of 'mixed beam therapy' (2/5 neutrons and

3/5 photons) in order to supplement the poorly penetrating neutrons with better penetrating photons with acceptable morbidity. Encouraging results were obtained in salivary gland and prostate cancers (27, 29).

The results of the clinical trials with neutrons under adverse treatment conditions provided the impetus for the NCI to initiate plans for the development of four high energy hospital-based neutron generators in 1979. The University of Washington was one of these sites of development, and serves as a model for discussion of characteristics of a modern neutron facility which result in improved treatment capabilities. Scanditronix Corporation of Uppsala, Sweden, was subcontracted to design and build the University of Washington facility. This machine utilizes a cyclotron to deliver 50 MeV protons to a gantry-mounted beryllium target, producing a neutron beam with an average energy of 22 MeV. The gantry design allows isocentric treatment through 360 degrees of rotation. Collimation is provided with an infinitely variable multi-leaf collimator, with wedges available internally within the gantry head. There is also an x-ray source for portal imaging within the gantry head. The features of this neutron unit provide the components necessary for optimal delivery of radiotherapy by modern standards.

Another factor in the optimization of neutron radiotherapy is a computerized three-dimensional treatment planning system which is compatible with the treatment unit. Three-dimensional treatment planning has been utilized on a regular basis at the University of Washington for patients undergoing neutron radiotherapy. Its usefulness has been exemplified in the treatment of unresectable arteriovenous malformations (AVMs) and salivary gland tumors using specialized techniques (30–33).

Neutron radiosurgery for intracranial arteriovenous malformations

From February 1987 through August 1989, 20 patients with inoperable intracranial AVMs were treated with neutron radiosurgery (30, 31). This technique involved a single dose of 9 Gy delivered through 7–9 non-opposing portals. Three-dimensional treatment planning was undertaken with pretreatment computerized tomography (CT), magnetic resonance imaging (MRI), and angiogram for AVM localization. A thermoplastic mask, specially designed to be bolted to the cyclotron treatment table, was used during the CT and MRI studies. This allowed for the intercomparison for all imaging information within the same format. Via magnetic tape, the CT study was loaded onto the three-dimensional treatment planning software system (UW-PLAN). Multiple isocentric fixed treatment portals were then designed using the 'beam's-eye-view' capabilities of the software. This allowed for the customization of individual fields using the cyclotron's multi-leaf collimator system. Each of these fields was shaped to correspond to the configuration of the AVM as it projected in the perspective of the treatment gantry relative to the patient. Vital structures could also be visualized and excluded from each field.

Although the overall response for the AVMs treated on this study was poor (42% partial response, no complete responses), there was no radiation-induced brain toxicity detectable clinically or on T2 weighted MRI. The absence of brain toxicity even with this relatively large non-fractionated dose of neutron radiation attests to the excellent dose distributions which were achievable with this system. Furthermore, this system of precise treatment delivery is likely to be useful for future endeavors involving boron neutron capture for radiosensitization in the treatment of malignant gliomas. A review of the potential therapeutic gain using boron neutron capture therapy is presented in this issue (34).

A three-field technique for treatment of parotid malignancies

Another example of the capabilities of a modern neutron radiation facility is the development of a 'three-field' technique for treatment of adenoid cystic carcinoma of the parotid gland (32). With the potential for these tumors to spread perineurally to the base of the skull, radiation volumes need to be large. Generally these fields extend superiorly to the base of skull to include the zygoma and two-thirds of the ear, posteriorly to include the posterior cervical lymph nodes and the mastoids, anteriorly to include the masseter muscle and two-thirds of the cheek, and inferiorly to include the hyoid bone, providing adequate coverage of potential submandibular nodal involvement. Using the conventional wedge pair technique, it is difficult to maintain tolerable neutron radiation doses to vital structures such as the contralateral parotid, contralateral eye, and brain tissue. Consequently, the 'three-field' technique was developed in order to adequately spare these normal tissues while achieving an adequate dose to tumor.

The 'three-field' technique first involves head immobilization with a thermoplastic mask and a CT scan for entry into the computerized three-dimensional treatment planning system as described above. The patient is then simulated with the intent of defining three fields—an ipsilaterallarge field, an ipsilateral intermediate field, and a contralateral small field (Fig. 4). The large ipsilateral field includes the primary tumor, posterior cervical nodes, and submandibular nodes. The superior border of the larger field includes the base of skull, but the multi-leaf collimator system is used to shield the optic nerves, optic chiasm, and other brain tissue which is not necessary for inclusion within the field. The intermediate ipsilateral field matches all parameters of the large ipsilateral field, but does not include the submandibular nodes and the anterior–inferior neck. The submandibular nodes and anterior–inferior neck are treated with an opposing contralateral small field. This contralateral small field is arranged such that it spares

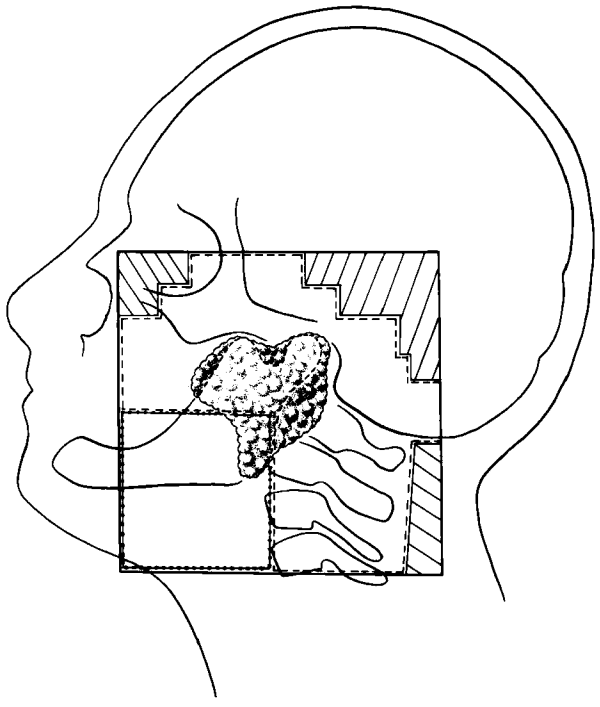

Fig. 4. Diagram of the three-field technique for treatment of parotid malignancies with neutron radiotherapy. The large ipsilateral field is shown as the solid line. The ipsilateral intermediate field is shown as the dashed line. The contralateral small field is shown as the solid line with dots. Blocking with the variable multi-lead collimator is designated by the hashed regions.

a significant portion of the contralateral parotid gland. To minimize the dose to the contralateral parotid gland, the two ipsilateral fields are normalized to the medial tumor volume, rather than to the isocenter at the patients midline. This normalization allows full dose to be delivered to the tumor bed with less than 35% of the full dose delivered to the contralateral parotid gland. The intent is to deliver as much of the prescribed total dose of 18–20 Gy through this three-field technique. The dose limiting structure with this technique is the spinal cord which is limited to a dose of 10 Gy. Subsequent fractions are delivered using a conventional technique, such as an ipsilateral wedged pair, to boost the tumor bed to the total planned dose. The result of this technique has been excellent local/regional tumor control with return of adequate salivary gland function 6–9 months after therapy.

Noncoplanar neutron beam therapy for minor salivary gland tumors

In addition to parotid gland malignancies, advances in neutron treatment planning and delivery have provided a means of treating minor salivary gland tumors involving the paranasal sinuses. Such tumors often require complex treatment plans due to the proximity of these tumors to vital structures, such as the eyes, optic pathways, and brain. Treatment planning is particularly difficult for treatment of adenoid cystic carcinoma in these sites with its propensity to spread by perineural routes. The University of Washington experience in treating adenoid cystic carcinomas of major and minor salivary glands has been reported (33), and provides another illustration of the effective treatment outcome achievable with a modern neutron radiation facility.

From 1984 through 1990, 34 patients with advanced (grossly unresectable primary and recurrent) adenoid cystic carcinomas were treated with fast neutron radiotherapy at the University of Washington. The treatment planning and delivery capabilities of this facility permitted non-orthogonal treatment planes and vertex fields necessary for optimal dose distributions in treating those patients with tumors of the paranasal sinuses. The results showed 100% local and local/regional control in 7 patients with paranasal sinus adenoid cystic carcinoma. These results in paranasal sinus tumors were comparable to those in major salivary gland adenoid cystic carcinomas, which had local and local/regional control of 92% and 83% respectively. Among these 7 patients with paranasal sinus tumors, there were two cases of serious late radiation toxicity (RTOG/EORTC grade III or IV). This incidence of severe toxicity was similar to that with treatment to other less challenging primary sites.

There are limited data reported on the local control of adenoid cystic carcinoma of the paranasal sinuses with conventional low LET radiotherapy or without surgery. Combining four series (6, 35–37), local control was achieved in 31% (12/39) patients with paranasal sinus adenoid cystic carcinoma receiving low LET radiotherapy. As with other sites, it appears that neutron radiotherapy offers a therapeutic gain relative to low LET radiation in minor salivary gland malignancies involving paranasal sites, and that modern facilities can deliver neutron radiotherapy effectively to these difficult locations.

Conclusions

Significant advances have taken place in modern neutron radiation facility design and integration with three-dimensional treatment planning systems. These advances have allowed neutron radiation dose delivery to achieve a level of sophistication equal to that of conventional photon radiation. The result has been improved local/regional control with acceptable morbidity.

Salivary gland malignancies have been presented as an example of a tumor type which appears to be more effectively treated with neutron radiotherapy compared to low LET radiation. Fast neutron radiotherapy is the 'treatment-of-choice' for patients with inoperable salivary gland tumours. Surgery should be limited to situations where clear margins can be achieved without significant morbidity. In particular, surgery should not sacrifice the facial nerve to achieve clear margins. For situations in which sacrifice of the facial nerve

appears necessary for adequate surgical margins, the patient should instead be referred for fast neutron therapy. Although the morbidity of skin reactions, fibrosis, and xerostomia appears somewhat higher with neutron radiotherapy than with low LET radiation, the benefit of improved local/regional control is not obviated.

REFERENCES

1. Conley J, Baker DG. Cancer of the salivary glands. In: Cancer of the Head and Neck. New York: Churchill Livingstone, 1981: 524–56.
2. Fitzpatrick PJ, Theriault C. Malignant salivary gland tumors. Int J Radiat Oncol Biol Phys 1988; 15: 613–7.
3. Vikram B, Strong EW, Shah JP, Spiro RH. Radiation therapy in adenoid-cystic carcinomas. Int J Radiat Oncol Biol Phys 1984; 10: 221–3.
4. Borthne A, Kjellevold K, Kaalhus O, Vermund J. Salivary gland malignant neoplasms: treatment and prognosis. Int J Radiat Oncol Biol Phys 1986; 12: 747–54.
5. Rafla S. Malignant parotid tumors: natural history and treatment. Cancer 1977; 40: 136–44.
6. Fu KK, Leibel SA, Levine ML, Friedlander LM, Boles R, Phillips T. Carcinoma of the major and minor salivary glands: analysis of treatment results and sites and causes for failures. Cancer 1977; 40: 2882–90.
7. Stewart JG, Jackson AW, Chew MK. The role of radiation therapy in the management of malignant tumors of the salivary glands. AJR Am J Roentgenol 1968; 102: 100–8.
8. Ellis ER, Million RR, Mendenhall WM, Parsons JT, Cassisi NJ. The use of radiation therapy in the management of minor salivary gland tumors. Int J Radiat Oncol Biol Phys 1988; 15: 613–7.
9. Dobrowsky W, Schlappack O, Karcher KH, Pavelka R, Kment G. Electron beam therapy in the treatment of parotid neoplasm. Radiother Oncol 1986; 6: 293–9.
10. Shidnia H, Hornback NB, Hamaker R, Lingeman R. Carcinoma of major salivary glands. Cancer 1980; 45: 693–7.
11. Guillamondi OM, Byers RM, Luna MA, Chiminazzo H, Jesse RH, Fletcher GH. Aggressive surgery in the treatment for parotid cancer: the role of adjunctive postoperative radiotherapy. AJR Am J Roentgenol 1975; 123: 49–54.
12. Elkon D, Colman J, Hendrickson FR. Radiation therapy in the treatment of malignant salivary gland tumors. Cancer 1978; 41: 502–6.
13. Ravasz LA, Terhaard CHJ, Hordijk GJ. Radiotherapy in epithelial tumors of the parotid gland: case presentation and literature review. Int J Radiat Oncol Biol Phys 1990; 19: 55–9.
14. Rossman KJ. The role of radiation therapy in the treatment of parotid carcinomas. AJR Am J Roentgenol 1975; 123: 492–9.
15. Wang CC, Goodman M. Photon irradiation of unresectble carcinomas of salivary glands. Int J Radiat Oncol Biol Phys 1991; 21: 569–76.
16. Saroja KR, Mansell J, Hendrickson FR, Cohen L, Lennox A. An update on malignant salivary gland tumors treated with neutrons at Fermilab. Int J Radiat Oncol Biol Phys 1987; 13: 1319–25.
17. Catterall M, Errington RD. The implications of improved treatment of malignant salivary gland tumors by fast neutron radiotherapy. Int J Radiat Oncol Biol Phys 1987; 13: 1313–8.
18. Buchholz TA, Laramore GE, Griffin BR, Koh WJ, Griffith TW. The role of fast neutron radiation therapy in the ma agement of advanced salivary gland malignant neoplasms. Cancer 1992; 62: 2779–88.
19. Batterman JJ, Mijnheer BJ. The Amsterdam fast neutron therapy project: a final report. Int J Radiat Oncol Biol Phys 1986; 12: 2093–9.
20. Duncan W, Orr JA, Arnott SJ, Jack WJC. Neutron therapy for malignant salivary glands. A report on the Edinburgh experience. Radiother Oncol 1987; 8: 97–104.
21. Maor MH, Hussey DJ, Fletcher GH, Jesse RH. Fast neutron tradiotherapy for locally advanced head and neck tumors. Int J Radiat Oncol Biol Phys 1981; 7: 155–63.
22. Ornitz R, Herskovic A, Bradley E, Deyenad JA, Rogers CC. Clinical observations of early and late normal tissue injury and tumor control in patients receiving fast neutron irradiation. In: Barendsen GW, Broerse J, Breur K. eds. High LET radiations in clinical radiotherapy. New York: Pergamon Press, 1979: 43–50.
23. Eichhorn HJ. Pilot study on the applicability of neutron radiotherapy. Radiobiol Radiother 1981; 3: 262–92.
24. Skolyszewski J, Byrski E, Chrzanowska A, et al. A preliminary report on the clinical application of fast neutrons in Krakow. Int J Radiat Oncol Biol Phys 1982; 8: 1781–6.
25. Batterman JJ, Breur K, Hart GAM, van Peperzeel HA. Observations on pulmonary metastases in patients after single doses and multiple fractions of fast neutrons and cobalt-60 gamma rays. Eur J Cancer 1981; 17: 539–48.
26. Laramore GE, Krall JM, Griffin TW, et al. Neutron vs photon irradiation for unresectable salivary gland tumors: final report of an RTOG-MRC randomized clinical trial. Int J Radiat Oncol Biol Phys 1993 27: 235–40.
27. Griffin TW, Pajak TF, Laramore GE, et al., Neutron vs photon irradiation of inoperable salivary gland tumors—Results of an RTOG-MRC cooperative randomized study. Int J Radiat Oncol Biol Phys 1988; 15: 1085–90.
28. Griffin TW. Fast neutron radiation therapy. Crit Rev Oncol Hematol 1992; 13: 17–31.
29. Laramore FE, Krall JM, Thomas FJ, et al. Fast neutron radiotherapy for locally advanced prostate cancer—Final report of a Radiation Therapy Oncology Group Randomized Clinical Trial. Am J Clin Oncol 1993; 16: 164–7.
30. Stelzer K, Griffin B, Eskridge J, et al. Results of neutron radiosurgery for inoperable arteriovenous malformations of the brain. Med Dosim 1991; 16: 137–41.
31. Griffin BR, Hummel-Warcola S, Mayberg MR, Eenmaa J, Eskridge J, Winn HR. Stereotactic neutron radiosurgery for arteriovenous malformations of the brain. Med Dosim 1988; 13: 179–82.
32. Hummel SM, Buchholz TA, Laramore GE. Treatment of adenoid cystic carcinoma of the salivary gland, a three-field technique. Med Dosim 1990; 15: 99–105.
33. Buchholz TA, Shimotakahara SG, Weymuller EA, Laramore GE, Griffin TW. Neutron radiation for adenoid cystic carcinoma of the head and neck. Arch Otolaryngol Head Neck Surg 1993; 119: 747–52.
34. Buchholz TA, Laramore GE, Wootton P, Enhancement of fast neutron beams with boron neutron capture therapy. A mechanism for achieving a selective, concomitant tumor boost. Acta Oncol 1994; 3:
35. Dal Maso M, Lippi L. Adenoid cystic carcinoma of the head and neck—A clinical study of 37 cases. Laryngoscope 1985; 95: 177–81.
36. Parsons JT, Mendenhall WM, Mancusco AA, Cassisi NJ, Million RR. Malignant tumors of the nasal cavity and ethmoid and sphenoid sinuses. Int J Radiat Oncol Biol Phys 1988; 14: 11–22.
37. Tran L, Sidrys J, Horton D., Sadeghi A, Parker PG. Malignant salivary gland tumors of the paranasal sinuses and nasal cavity. Am J Clin Oncol 1989; 12: 387–92.