

Neutron and Photon Radiation Medical Studies (Updated 2009)

NEUTRON MEDICAL PAPERS

(1)

Neutron Therapy and Specific Ionization

R.S. Stone

1948 Am. J. Roentgenol

(2)

Observations on pulmonary metastases in patients after single doses and multiple fractions of fast neutrons and cobalt-60 gamma rays.

J.J. Batterman, K Breur et al

1981 European Journal of Cancer

(3)

Fast neutron radiotherapy for inoperable salivary gland tumors: Is it the treatment of choice?

George Laramore, PhD MD

1987 Radiation Oncology Biologic Physics

CONCLUSION: "I believe that one can indeed conclude that fast neutron radiotherapy is the present "treatment of choice" for inoperable malignant tumors of the salivary glands."

STATISTICAL CONCLUSIONS: "From multiple studies, 188 patients treated with photon or electron treatment had 52 patients achieve local control (28%), while 267 patients treated with neutrons had 182 patients achieve local control (68%). From a clinical trial jointly sponsored by the EORTC AND RTOG for 25 evaluable patients at one year the overall local/regional control rate was 53% for the neutron arm and 31% on the photon arm. The actuarial survival at 2 years was 55% for the neutron group and 13% for the photon group."

(4)

Neutron vs. Photon irradiation of inoperable salivary gland tumors: results of a TROG-MRC cooperative randomized study

T.W.Griffin, MD, T.F. Pajak, PhD, G.E. Laramore, PhD MD, et al

1988 U of Washington, Seattle WA

CONCLUSION: "Although not statistically significant, the neutron-treated patients tended to show more toxicity (side-effects, complications) than the photon-treated patients... Taken as a whole, the data from the radiobiological studies, the non-random clinical studies and the prospective randomized clinical trial reported here overwhelmingly support the contention that fast neutron radiotherapy offers a significant advance in the treatment of inoperable and unresectable primary and recurring malignant salivary gland tumors."

STATISTICAL CONCLUSIONS: "32 patients with inoperable, recurrent or unresectable malignant salivary gland tumors were entered on a randomized RTOG/MRC study comparing fast neutron therapy with conventional photon therapy... 17 to receive neutron and 15 to receive photon therapy. The complete tumor clearance rates at the primary site were 85% (11/13) for neutrons and 33% (4/12) for photons following protocol treatment ($p=0.01$). With two years minimum follow-up, the loco/regional tumor control advantage of 67% for neutrons vs. 17% for photons is statistically significant at the $p<0.005$ level. There is a strong trend favoring neutrons in terms of survival as well (62% vs. 25% at the $p = 0.10$ level)."

(5)

The role of fast neutron radiation therapy in the management of advanced salivary gland malignant neoplasms

Thomas Buchholz, MD, George Laramore, PhD MD, et al

1991 U of Washington, Seattle WA

CONCLUSION: "Although these tumors have historically have been considered to be resistant to low-LET radiation, sufficient information has accumulated to indicate that postoperative photon radiation improves local control rates in patients at high risk of residual microscopic disease...Our series supported the conclusive evidence showing superior local control rates achievable with neutron therapy compared with low-LET radiation in the treatment of salivary gland tumors that were inoperable or recurrent or had gross residual disease after surgery.

STATISTICAL CONCLUSIONS: "Summary of local control rates for malignant salivary gland tumors treated with low linear energy transfer radiation therapy. 13 studies totaling 299 patients treated *de novo* and for gross disease after a post-surgical recurrence, but not patients who were treated postoperatively for microscopic residual disease: 79 of 299 achieved local control (26%)."

"Summary of local control rates for malignant salivary gland tumors treated with neutron radiation therapy. 9 studies totaling 309 patients treated *de novo* and for gross residual disease after a post-surgical recurrence but not patients who were treated postoperatively for microscopic residual disease: 207 of 309 achieved local control (67%)."

(6)

Metastatic adenoid cystic carcinoma of salivary glands: case reports and review of the literature

George Laramore PhD MD

1996 U of Washington Medical Center, Seattle, WA

CONCLUSION: "Fast neutron radiotherapy is now widely regarded as the most effective form of treatment for patients with locally advanced/unresectable adenoid cystic carcinomas of major and minor salivary glands. At the University of Washington, we annually treat 70+ patients with advanced salivary gland malignancies (adenoid cystic carcinoma and other histologies)."

(7)

Ten years of fast neutron therapy in Munster

F.J. Prott, U. Haverkamp, et al

1996 Westfälische Wilhelms University, Munster, Germany

CONCLUSION: "After 10 years of neutron therapy in Munster, high effectivity can be ascribed to neutron therapy in case of adenoid cystic carcinoma, soft tissue sarcoma and recurrent rectal carcinoma. In particular, the high rate of complete remission and the improved overall survival of the 64 patients treated for adenoid cystic carcinoma shows the superiority of this treatment modality compared to photon therapy alone...From our experience, unresectable adenoid cystic salivary gland tumors seem to be an absolute indication for neutron radiation therapy..."

STATISTICAL CONCLUSIONS: "269 patients were treated with neutrons between 1985 and 1995. The 64 patients with Adenoid Cystic Carcinomas of the salivary glands had either an unresectable primary tumor, an unresectable recurrence or residual tumor after surgery. Results from this present study indicated a 61% local control rate. The lower result from Munster could be...by the fact that only 62% of the patients could be treated with potentially curative intent, while 23% suffered from extremely advanced recurrent tumors only allowing for palliative treatment. Referring to the literature, particular interest should be focused on a comparison with the results of photon therapy alone in Adenoid Cystic Carcinoma. On average, complete

remission could be achieved in only 28% of the patients in contrast to neutron therapy with a mean remission rate of 67%.”

(8)

European results in neutron therapy of malignant salivary gland tumors

A Krull, R. Schwartz, et al

1996 Multiple sites in Europe

Germany: Hamburg, Heidelberg, Berlin, Munich France: Orlean

CONCLUSION: “In summary, neutron therapy offers a therapeutic gain factor compared to low-LET radiation and should be the treatment of choice in both cases of advanced salivary gland malignancies which are inoperable or not completely resected, and in recurrent disease.”

STATISTICAL CONCLUSION: “In Europe to date, 501 patients with salivary gland tumors have been treated with neutrons alone or with combined modalities...The pooled data of some international series for low linear transfer radiation show a local control of 28%. Especially in advanced tumors, neutron therapy can improve local control and should be the treatment of choice. The clinical data from different therapy centers in Europe show local control of 67% in gross disease.”

(9)

Neutron radiotherapy for adenoid cystic carcinoma of minor salivary glands

James Douglas, MD, George Laramore PhD MD, Mary Austin-Seymour, MD, et al

1996 U of Washington Medical Center, Seattle, WA

CONCLUSION: “Neutron radiation offers high local-regional control and survival rates for locally advanced, unresectable, and/or recurrent adenoid cystic carcinomas of minor salivary glands, and should be considered as initial primary treatment for these patients.”

STATISTICAL CONCLUSIONS: “84 patients having Adenoid Cystic Carcinoma of minor salivary glands were treated with fast neutron radiotherapy during the years of 1985-1994. All patients had either unresectable disease or gross residual disease remaining after attempted surgical extirpation. 17 patients had previously received conventional radiotherapy and their subsequent treatment fields and doses for neutron radiotherapy were modified for critical sites (brainstem, spinal cord, brain). The 5 year actuarial local-regional tumor control rate for all patients treated with curative intent was 47%.”

(10)

Neutron Radiotherapy for the treatment of locally advanced major salivary gland tumors

James Douglas, MD, MS, Shawn Lee, MD, George Laramore PhD MD, Mary Austin-Seymour, MD, et al

1998 U of Washington Medical Center, Seattle, WA

CONCLUSION: “Neutron radiotherapy, thus, is an effective form of therapy for patients with high risk tumors of major salivary gland origin. Survival remains suboptimal largely because of the development of distant metastases.”

STATISTICAL CONCLUSIONS: “148 patients with malignant salivary gland tumors of major salivary gland origin (32% with Adenoid Cystic Carcinoma) were treated with fast neutrons between the years of 1984 and 1995. The 5 year actuarial locoregional control rate for all patients with gross tumor treated with curative intent was 59%.”

(11)

Results of fast neutron therapy of adenoid cystic carcinoma of the salivary glands

R. Potte, F.J. Prott, et al

1999 University of Vienna, Austria

CONCLUSION: According to this experience and taking into account the so far collected experience, fast neutron radio-therapy remains the treatment of choice for large and unresectable primary and recurrent ACC, and residual disease after surgery.”

STATISTICAL CONCLUSIONS: “72 consecutive patients with ACC were treated with fast neutrons. Complete response was achieved in 28 patients, partial response in 35 patients. Local control was observed in 73.4% after a mean observation period of 36 months.”

(12)

The role of high-let radiotherapy compared to conformal photon radiotherapy in adenoid cystic carcinoma

J. Debus, R. Engenhart-Cabillic, et al

1999 Heidelberg, Germany

CONCLUSION: “A critical review of the literature provides evidence that high-LET radiotherapy offers a therapeutic gain factor compared to low-LET radiation and should be the treatment of choice in advanced salivary gland malignancies, which are inoperable or not completely resected, and in recurrent disease. Modern techniques of conformal high LET radiotherapy, e.g. heavy ion beam radiotherapy, will help to reduce the long and short term toxicity of radiotherapy.”

(13)

Use of fast neutrons in the treatment of tumors of the salivary glands: rationale, review of the literature and experience in Orleans

N. Breteau, N. Wachter , et al

2000 Radiotherapie et Hematologie Clinique Orleans France

CONCLUSION: “Taken as a whole the data from the radiobiologic studies, the results of the historical clinical studies and the prospective randomized clinical trial overwhelmingly support the contention that neutrontherapy offers a significant advance in the treatment of inoperable and unresectable primary and recurrent malignant salivary gland tumors.”

STATISTICAL CONCLUSIONS: “In this survey, all the patient series treated worldwide were reviewed. They show an overall control rate of 31% with photon vs 64% with neutron therapy. In Orleans, since 1987, 59 patients have been treated. At 5 years the persistent local control probability was 69.5%, the 5-year crude survival probability 66% and the 5-year tumor free survival probability was 64.5%.”

(13A)

Recent improvements and operational status of the Seattle clinical cyclotron facility

R. Risler, S. Banerian, R.C. Emery, I.Kalet, G.E. Laramore and D.Reid

University of Washington Medical Center, Seattle WA

Cyclotrons and Their Applications 2997, Eighteenth International Conference

CONCLUSION: “The clinical cyclotron at the University of Washington Medical Center continues to work reliably. While neutron therapy use has declined somewhat, the demand for other uses, in particular for radionuclide production with alpha particles is increasing. The first components of a new control system are now operational and further upgrades are in progress.

Photon Studies

(14)

Salivary neoplasms: Overview of a 35-year experience with 2,807 patients

Ronald Spiro, MD

1985 Sloan Kettering New York

CONCLUSIONS: "Currently, many of our patients with malignant tumors are receiving adjunctive postoperative irradiation to the primary site and neck. Recent reports from other centers suggest that this has significantly reduced locoregional recurrence. Patients with Stage III disease, inadequate surgical margins, or ominous histologic findings such as anaplastic carcinoma or extensive perineural infiltration are obvious candidates for combined therapy."

STATISTICAL CONCLUSIONS: "Of the 2807 patients studied, 1278 had malignant neoplasms, and of those 1278, 270 had ACC. Of these 270, approximately 50% survived 10 years, and the trend towards better survival in patients with intermediate or low grade tumors disappeared when the follow-up approached or exceeded 10 years."

(15)

Photon radiation of unresectable carcinomas of salivary gland

C.C. Wang, M.D., Max Goodman, M.D.

1991 Harvard Medical School, Boston MA

CONCLUSIONS: "Recent reports summarized the results of treatment among various radiation centers as published in the literature, and indicated that the local control rates for inoperable cancers of the parotid gland after neutron irradiations were superior to those after conventional photon irradiation, that is, 68% (range 38%-81%) versus 28% (range 2%-54%), respectively.

Significant radiation complications after neutron irradiation occurred in 1 of 6 patients treated."

"Although the numbers in the series were small and the follow-up relatively short, our experience suggested that state of the art photon radiation therapy using the b.i.d. program can achieve good local control of unresectable salivary gland tumor and the local control rates were comparable to those claimed by neutron therapy yet without significant radiation therapy complications."

STATISTICAL CONCLUSIONS: "24 salivary gland patients were treated between 1980 and 1989 with various photon techniques. Of the 24 patients, 7 had Adenoid Cystic Carcinoma. For the complete group, the 5-year actuarial local control of parotid gland lesions after photon radiation was 100% and the survival rate was 65%. For the minor salivary gland lesions, the 5-year actuarial local control was 78% and the survival rate with or without disease was 93%."

(16)

Adenoid cystic carcinoma of the salivary glands: a review of 10 years

R.K. Sur, B. Donde (MD?)

1995 African Institute of Medical Research, Johannesburg, South Africa

CONCLUSIONS: "Adenoid Cystic Carcinomas are slow-growing tumors. Whenever possible, total surgical resection must be attempted. Postoperative photon radiotherapy improves local control and disease-free survival without altering overall survival... There is a role for neutron radiotherapy in advanced cases, as has been published recently."

(16) (continued from above)

Adenoid cystic carcinoma of the salivary glands: a review of 10 years

STATISTICAL CONCLUSIONS: "Between January 1, 1983 and December 31, 1992 a total of 50 patients with ACCs arising from the salivary glands were seen...11 patients had complete surgical excision and did not receive any radiotherapy...23 had microscopic residual...16 patients refused surgery or had advanced tumors making surgical resection impossible. 32 patients had radiotherapy...to a median dose of 60 Gy...two patients received neutron therapy (doses 20.4 and 26 Gy). The disease-free survival...was 26% for 5 and 10 year follow-up. The overall survival...at 5 years was 38% and at 10 years, 29%. The local control at 5 and 10 years was 30% with most recurrences occurring in the first 3 years."

(17)(18)

The influence of positive margins and nerve invasion in adenoid cystic carcinoma of the head and neck treated with surgery and radiation

A.S. Garden, MD, R.S. Weber, MD

1995 MD Anderson Cancer Center, Houston TX

STATISTICAL CONCLUSIONS(17): Between 1962 and 1991, 198 patients...with adenoid cystic carcinoma of the head and neck received postoperative radiotherapy for known or suspected microscopic residual disease following surgery. "1. Local control rates for patients with adenoid cystic carcinomas treated with surgery and postoperative radiation for suspected microscopic residual were excellent, with an actuarial control rate of 10 years of 86%. 2. The presence of perineural invasion of small unnamed nerves did not correlate with worse control. Positive margins and named nerve involvement were associated with an increased risk of local failure in our patients treated with surgery and radiation. Yet even in the worst scenario, when both features were present, the control rate at 10 years was 70%. 3. Patients receiving 50-55 Gy, particularly if they had positive margins, had worse local control, and we recommend a minimum of 60 Gy to the original tumor volume, and 66 Gy if multiple margins are positive or there is extensive soft tissue involvement."

CONCLUSIONS(18): "Excellent local control rates were obtained in this population using surgery and postoperative radiotherapy and we recommend this combined approach for most patients with adenoid cystic carcinomas of the head and neck. Perineural invasion was an adverse prognostic factor only when a major (named) nerve was involved. Microscopic positive margins was also an adverse prognostic factor, but even when present, local control was achieved in over 80% of our patients."

(19)

Management of minor salivary gland carcinomas

J.T. Parsons M.D., Wm. Mendenhall, M.D.

1996 U of Florida College of Medicine, Gainesville, Florida

CONCLUSIONS: "Treatment of minor salivary gland carcinomas is usually by combined surgery and radiotherapy, but there are situations where surgery alone or radiotherapy alone may be used. The ability to control these tumors with radiotherapy alone is not widely recognized."

STATISTICAL CONCLUSIONS: "Between October 1964 and November 1992, 95 patients with minor salivary gland carcinomas of the head and neck received radiotherapy. Contrary to the widely held belief that local recurrence after radiotherapy eventually develops in all patients with adenoid cystic carcinoma, local control has been maintained in 13 patients after radiotherapy alone; 5 of the 13 patients have been observed for 10 to 17 years."

(20)

Postoperative radiotherapy for malignant tumors of the parotid gland

Adam Garden MD, William Morrison MD

1996 M.D. Anderson Cancer Center, Houston, TX

CONCLUSIONS: "In conclusion this updated retrospective study of postoperative radiation for parotid gland carcinomas has reaffirmed the excellent control rates obtained in previous analysis. A large cohort has been treated with an ipsilateral electron beam technique and severe complications were infrequent...Late complications of varying degrees of severity developed in 37 patients (22%)."

STATISTICAL CONCLUSIONS: "A retrospective analysis of 166 patients treated between 1965-1989 was performed. 27 patients (16%) had Adenoid Cystic Carcinoma. All patients were treated following surgery and did not have macroscopic disease at the time of their radiation. The actuarial 2-, 5-, and 15- year survival rates were 89, 78, 60, and 52%, respectively."

(21)

Potential clinical efficacy of intensity-modulated conformal therapy

S.L Meeks MD, J.M Buattie MD

1997 U of Florida College of Medicine, Gainesville, Florida

CONCLUSIONS: "Using the entire 3D data set to construct radiotherapy plans through virtual simulation is always advantageous, whether done for stereotactic radiosurgery, beams-eye-view conformal therapy, or intensity-modulated conformal treatment. Intensity modulation of the photon beam further enhances treatment planning under specific conditions. In general, the intensity-modulated technique is advantageous for large, irregular targets with critical structures in close proximity. Intensity-modulated treatment does not appear advantageous for stereotactic radiosurgery or treatment of the intact breast."

(22)

Improved results with accelerated hyperfractionated radiotherapy of advanced head and neck cancer

Felix Leborgne MD, Eduardo Zubizarreta MD et al

1999 Int. J. Cancer (Radiat. Oncol. Invest.)

CONCLUSIONS: "This study has shown that accelerated hyperfractionated irradiation using two doses of 1.6 Gy each treatment day for less than 6 weeks in advanced head and neck cancer in male patients provides significantly better local tumor control and cause-specific disease-free survival, without increased morbidity, than conventional fractionation delivered at the previously relaxed overall times of 7 weeks, but sometimes exceeding 8 or 9 weeks."