LITERATURE REVIEW:

THE ROLE OF RADIATION THERAPY IN AIDS-ASSOCIATED KAPOSI SARCOMA

Radiation therapy is considered to be the palliative modality of choice in the treatment of AIDS- associated Kaposi sarcoma as the lesions are radioresponsive and radiation therapy provides good palliation.

Cooper et al. (20) treated 38 patients with epidemic Kaposi sarcoma with radiation therapy in order to define the role of radiation therapy in the management of this disease. Between July 1981 and June 1985, 47 sites were treated. Radiation therapy technique used varied with characteristics of the treated lesion. Dose fractionation regimens used varied from 8 Gy single fraction to 30 Gy in 10 fractions. Patients were followed-up for a range of 0 – 43 months. Objective treatment response was assessed in 43 sites. Complete response was documented in 22 sites, complete response with residual pigmentation in 11 sites, partial response in 5 sites and no response in 5 sites. Subjective treatment response was assessed in 26 sites. Complete pain relief occurred in 14 sites, partial response in 3 sites and no change in 4 sites. Severe mucositis occurred in all 4 patients who received radiation therapy to oral cavity lesions at low doses, which ranged from 7.5 Gy at 1.5 Gy per fraction to 27 Gy at 3 Gy per fraction. Minor cases of pain and blistering were noted in 2 of 7 patients who received radiation to the feet. The study concluded that the role of radiation therapy in the management of epidemic Kaposi sarcoma is palliative. Treatment technique and

dose should be individualized but regimens ranging from 8 Gy single fraction to 30 Gy in 10 fractions were effective with minimal morbidity.

Spittle (33) treated 17 patients with radiation therapy for AIDS-associated Kaposi sarcoma and reported the results. Dose fractionation regimens used ranged from 6 Gy single fraction to 16 Gy in 4 fractions. Partial responses were documented in all cases. No cases of toxicity were reported. The author concluded that radiation therapy for AIDS-associated Kaposi sarcoma improves function and cosmesis.

Cooper et al. (34) treated 129 patients with radiation therapy for epidemic Kaposi sarcoma in order to determine if any association existed between the indications for treatment and treatment outcomes. Between 1 July 1981 and 31 December 1988, 226 lesions were treated for the indications of pain (n=100), cosmesis (n=73), oedema (n=22), impaired function (n=10), ulceration (n=9), local control of a mass (n=8) and bleeding (n=4). Radiation therapy technique used varied with the lesion characteristics. Localized lesions (n=186) were treated with either 6 MeV electrons or 94 kVp x-rays to a dose of 30 Gy in 10 fractions over 2 weeks. Extensive lesions were treated with 6 – 8 MV photon therapy and a dose of 8 Gy in a single fraction. Treatment response was assessed in the short-term and long-term. The short-term complete response rate was 68% within 1 month of treatment. Of these complete responses, 20% had residual pigmentation. The long-term complete response rate was 62%. The

overall complete response rate was 68%. The rate of local recurrence was 9%. The authors concluded that the response of epidemic Kaposi sarcoma to radiation therapy, both in the short term and the long term, is influenced by treatment intent, site of the lesion and patients' Karnofsky performance score.

Nobler et al. (14) retrospectively reviewed 33 patients with the Acquired Immune Deficiency Syndrome (AIDS) treated with radiation therapy to 106 sites between January 1983 and June 1985, in order to describe the natural history of AIDS and to define the role of radiation therapy in such patients. The study population comprised 26 patients diagnosed with only Kaposi sarcoma, 2 patients diagnosed with only malignant lymphoma and 3 cases with both Kaposi sarcoma and malignant lymphoma. The radiation therapy technique used varied with lesion characteristics. Patients received doses of 1.8 to 3 Gy per fraction daily for 1 to 2.5 weeks in the treatment of Kaposi sarcoma lesions and for 3 to 5 weeks for the treatment of malignant lymphomas. All of the treated lesions showed fair to excellent treatment responses. Kaposi sarcoma lesions were noted to recur in clusters at the margins of previously treated fields. The average survival was 8.7 months. The study advocates the frequent use of radiation therapy in patients with AIDS for effective palliation and recommends the use of palliative doses of 15 Gy to 22 Gy in the treatment of Kaposi sarcoma.

Chak et al. (35) treated 24 patients with AIDS-associated Kaposi sarcoma with radiation therapy in order to confirm the palliative role of radiation therapy in the

management of this disease and to describe treatment toxicity. Between July 1985 and January 1987, 72 sites of Kaposi sarcoma were treated with 80 courses of radiation therapy. The radiation therapy technique used was determined by lesion characteristics. The radiation dose administered was 20 Gy in 10 fractions over a period of 2 weeks. The overall median survival was reported as 7 months post irradiation. A complete or partial response was observed in 46 of 53 lesions. Oedema did not respond well to radiation therapy. Symptomatic control was maintained for a median follow-up duration of 7 months. Pain was well controlled, with maximum pain relief being reported within 1 to 2 weeks. Symptoms recurred in 7 sites. Oral mucositis occurred in 9 cases with doses ranging from 12 Gy in 6 fractions to 18 Gy in 9 fractions. Patients treated to lesions on the foot experienced intense skin erythema, episodes of generalized pain and desquamation of the skin on the sole in 5 of 7 cases. The study concluded that radiation therapy did not cause the Kaposi sarcoma lesion itself to resolve but that it provided good palliation. The authors cautioned that significant toxicity at sites like the oral mucosa and the foot may limit the radiation therapy dose and consequently treatment efficacy.

Berson et al. (21) treated 187 patients with epidemic Kaposi sarcoma with radiation therapy in order to determine the indications for therapy, treatment outcome and toxicity. Between March 1982 and October 1987, 375 sites were treated. The radiation therapy technique used was determined by lesion characteristics. Treatment field sizes ranged from 4 cm^2 to total skin irradiation and the total treatment doses ranged from 8 Gy single fraction to 15 - 40 Gy in

5 - 10 fractions. The median follow-up of patients still alive was 11 months. The reported median survival was 15 months (range: 1 - 71 months). An overall response of 93% was achieved. Moderate grade 2 reactions occurred in 60 cases and severe grade 3 reactions occurred in 3 cases. The data showed that the 8 Gy single fraction regimen was associated with a significant decrease in high-grade toxicity ($p<0.001$). Severe mucositis occurred in the oral cavity when a high dose per fraction of 4 Gy was used. Reducing the dose per fraction to 1.8 – 2 Gy per fraction was associated with a decrease in toxicity. The reported median time to progression was 21 months and the actuarial freedom from relapse at 6 months was 69%. The study concluded that the role of radiation therapy in the management of epidemic Kaposi sarcoma is palliative and recommended the use of the 8 Gy single fraction regimen.

Geara et al. (36) retrospectively reported on 149 patients with AIDS-associated Kaposi sarcoma treated with radiation therapy to cutaneous lesions in order to determine the effectiveness of radiation therapy management of this disease. Patients were treated between June 1986 and December 1988 according to the lesion characteristics with electron beam extended field radiation (n=88) and 4 KV x-ray beam localized radiation therapy (n=61) either as definitive therapy or as a boost following extended field radiation therapy. Patients were treated to a total radiation dose of 30 Gy. Results were analyzed in 131 patients. The overall response rate was 93%. Complete response occurred in 63% and partial response in 30%. The results showed a trend to a higher

complete response rate with localized radiation, which was not statistically significant (p=0.08). The reported average time to local control was 1.5 months. The recurrence rate was 64% at an average of 5.5 months in patients with non-progressive AIDS. Significant treatment toxicity was minimal. Skin erythema occurred in 6% of cases, dry epidermitis in 60%, exudative epidermitis in 26% and exudative epidermitis with ulceration in 8%. The authors concluded that radiation therapy provides good palliation of pain, discomfort and improved cosmesis in patients with AIDS-associated Kaposi sarcoma. The use of localized radiation is recommended with extended field radiation being reserved for those cases in whom the use of localized radiation are not possible.

Piedbois et al. (18) treated 453 patients with epidemic Kaposi sarcoma with radiation therapy in order to determine the role of radiation therapy in this disease. Between June 1986 and June 1993, 5015 courses of radiation therapy were administered. Tumour site and size determined the radiation therapy technique used. Treatment fields were divided into 2 groups based on the site of the disease. Group 1 (n=1312) included disease of the conjunctiva (n=32), eyelid (n=306), lips (n=170), hands (n=208), feet (n=417), penis (n=131), oral mucosa (n=43) and anus (n=5). Group 2 (n=3703) included disease of the face (n=629), trunk (n=1593) and limbs (n=1481). Sites in group 1 received low dose radiation therapy of 2.5 Gy per fraction, 4 times per week to total doses of 10 – 20 Gy with the aim of inducing either a complete or partial remission. Sites in group 2 were treated with radiation therapy of 20 Gy given in 2 weeks followed by a 2 week break and thereafter a boost of 10 Gy in 1 week to a total dose of 30 Gy.

Extended radiation fields were treated with 4 MeV electrons while localized fields were treated with 45 – 100 KV x-rays for cutaneous lesions and 4 MV photons for oral mucosa lesions. Patients were followed-up for a mean of 7 months (range: 2 - 24 months). The results for group 1 were an overall objective response of 87.8% and an increased incidence of oral mucositis with 20% severe reactions documented in patients receiving 15.2 Gy. The objective response rate was 96% in group 2 and toxicity was reported as severe epidermitis with skin ulceration in 5%, exudative epidermitis in 26%, dry epidermitis in 60% and erythema in 9%. The overall recurrence rate was 71% after 7.5 months. Progressive AIDS and opportunistic infections were associated with 85% of recurrences. The study concluded that radiation therapy is an effective treatment for epidemic Kaposi sarcoma. The authors recommended doses of 15.2 Gy for oral mucosa lesions, 20 Gy for treatment of sites as in group 1 and 30 Gy for lesions of the skin.

Piccino et al. (37) retrospectively reviewed 65 patients with epidemic Kaposi sarcoma treated with radiation therapy in order to ascertain the role of radiation therapy in the management of this disease. Between 1986 and 1992, 594 lesions were treated with kilovoltage radiation. The radiation therapy treatment technique was individualized for each lesion. The mean follow-up was 9 months (range: 1 – 43 months). The reported complete response rate with residual pigmentation was 68.3%, complete response with good cosmesis was 17.7% and complete response with hypopigmentation was 0.5%. The partial response rate was 13.5%. Two cases of ulceration were noted at the treated sites on the lower limbs

at 1 and 4 months post irradiation respectively. The relapse rate was reported as 2.4% at 2 to 9 months post irradiation. The study concluded that radiation therapy is an effective treatment for epidemic Kaposi sarcoma with minimal morbidity.

Kirova et al. (19) retrospectively analyzed 643 patients treated with radiation therapy for AIDS-associated Kaposi sarcoma in order to define the role of radiation therapy in the management of this disease with regard to treatment efficacy, dose fractionation and toxicity. Between June 1986 and December 1996, 6777 sites were treated with either extended field or local field radiation therapy, according to lesion characteristics, to total doses ranging from 10 to 30 Gy. The mean follow-up was 8.2 months (range: 2 – 36 months). The reported overall objective response rate was 92%. Complete response occurred in 66% of cases and partial response in 26%. The average time to local control was 1.2 months. Mild skin reactions were noted in 8%, dry epidermitis in 61%, exudative epidermitis in 26% and exudative epidermitis with ulceration in 5%. At low total doses of 15 or 15.2 Gy mild mucosal reactions were recorded in 66% of cases, moderate reactions in 18% and severe reactions in 16%. In the treatment of lesions involving the eyelids, conjunctiva and genitalia, mild reactions occurred in 75.1% of cases, moderate reactions in 21% and severe reactions in 3.9%. The overall recurrence rate for cutaneous lesions was 71% after an average of 8 months while 15 cases of oral cavity lesions recurred after an average of 6 months. The authors concluded that radiation therapy was an effective treatment for AIDS-associated Kaposi sarcoma and recommended doses of 15 Gy for the

treatment of oral cavity lesions, 20 Gy for lesions involving the eyelids, conjunctiva and genitalia and local field radiation with a fractionated regimen to a total dose of 30 Gy for cutaneous lesions.

There is extensive literature available showing that Kaposi sarcoma lesions are radioresponsive with overall response rates ranging from 87-100% (Table 1). The reported toxicity was acceptable in all cases.

TABLE 1: RADIORESPONSIVENESS OF KAPOSI SARCOMA:

AUTHOR	SITES ASSESSED	DOSE	OVERALL OBJECTIVE RESPONSE (%)
Cooper 1987	43	8 – 30 Gy	88
Nobler 1987	106	9 – 39 Gy	100
Chak 1988	53	20 Gy	87
Berson 1990	375	8 – 40 Gy	93
Cooper 1991	226	8 – 30 Gy	68
Piedbois 1994	5015	10 – 30 Gy	87.8 – 96
Kirova 1998	6777	10 – 30 Gy	92

RADIATION THERAPY DOSE FRACTIONATION REGIMENS:

The optimal dose fractionation regimen for AIDS-associated Kaposi sarcoma is not known and many authors recommend that treatment be individualized for each patient.

Wit de, et al. (22) prospectively analyzed 31 patients diagnosed with AIDS-associated Kaposi sarcoma who were treated palliatively with 8 Gy single fraction radiation therapy in order to determine objective and subjective response rates and the duration of treatment response. Between October 1988 and August

1989, 74 fields were treated for the indications of comesis (n=38), pain (n=28) and oedema (n=8). The radiation therapy technique used varied with the lesion characteristics. Follow-up was done twice weekly for the first 2 months post therapy and thereafter monthly. An objective response was documented in 25 treatment fields (34%). Of these, complete response occurred in 6 fields and partial response in 19 fields. A subjective response was documented in 67 treatment fields (90%). Progressive disease within the treatment field and recurrence was documented in 23 of 36 treatment fields with a minimum follow-up of 4 months. The treatment was well tolerated with patients experiencing mostly grade 1 and 2 toxicity. The study concluded that the 8 Gy single fraction radiation therapy regimen is effective in the palliation of AIDS-associated Kaposi sarcoma in patients with a limited survival.

Stelzer et al. (16) compared 3 fractionation regimens in 14 patients with AIDS-associated Kaposi sarcoma, in terms of lesion characteristics, treatment outcome and toxicity in order to determine the optimal dose of radiation therapy for treatment response. Between May 1991 and June 1992, 71 sites were randomized to receive 8 Gy single fraction radiation therapy (n=24), 20 Gy in 10 fractions (n=24) or 40 Gy in 20 fractions (n=23). All sites were treated with 6 MeV electrons to the lesion with a 2 cm margin. The reported complete response rate was 83% with a total dose of 40 Gy, 79% with 20 Gy and 50% with 8 Gy (p=0.04). The rate of absent purple pigmentation was reported as 43% with 40 Gy, 8% with 20 Gy and 80% with 8 Gy (p=0.03). The rate of lesion failure was reported as 52% with 40 Gy, 67% with 20 Gy and 88% with 8 Gy (p=0.03). The

reported median time to treatment failure was 43 weeks with 40 Gy, 26 weeks with 20 Gy and 13 weeks with 8 Gy (p=0.003). Increased toxicity was documented with higher radiation therapy doses but was limited to grade 1 acute and late toxicities in all instances. The study concluded that treatment response and tumour control with radiation therapy management of AIDS-associated Kaposi sarcoma showed dose dependence.

Harrison et al. (24) prospectively compared 2 radiation therapy fractionation regimens in the treatment of AIDS-associated Kaposi sarcoma with regard to treatment response and cosmetic outcome. Between June 1990 and May 1994, 596 lesions in 57 patients were treated with either 16 Gy in 4 fractions (n=198) or 8 Gy single fraction (n=398). The mean follow-up was 19 weeks. The overall response rate for patients treated with 16 Gy in 4 fractions was 80.8% and 77.6% for those treated with 8 Gy single fraction. There was no statistical difference in response rates between the 2 groups (p>0.1). Grade 0 and 1 cosmesis was reported in 89.9% of patients treated with 16 Gy in 4 fractions and 87.1% in those treated with 8 Gy single fraction, which was not statistically different (p>0.5). A statistically significant advantage for the 8 Gy single fraction regimen was noted for pigmentation (p>0.001). The median survival was 17 months (range: 3 - 52 months). There was tumour recurrence in 109 lesions. The median duration of response was documented as 27 weeks (range: 10 – 87 weeks). The authors concluded that 8 Gy single fraction radiation therapy provided good treatment response with normal skin pigmentation in patients who have a short median life expectancy.

The studies of dose fractionation are summarized in Table 2 below.

TABLE 2: RADIATION DOSE FRACTIONATION REGIMENS:

AUTHOR	SITES ASSESSED	RADIATION REGIMEN	OVERALL OBJECTIVE RESPONSE	RECURRENCE RATE
De Wit 1990	74	8 Gy single fraction	34%	64%
Stelzer 1993	71	8 Gy single fraction	50%	88%
		20 Gy in 10 fractions	79%	67%
		40 Gy in 20 fractions	83%	52%
Harrison 1998	596	8 Gy single fraction	78%	18% (whole group)
		16 Gy in 4 fractions	81%	

RADIATION THERAPY TECHNIQUE IN KAPOSI SARCOMA:

There is a paucity of studies in the literature investigating radiation therapy treatment technique in patients diagnosed with AIDS-associated Kaposi sarcoma. Radiation therapy technique has been studied mostly in patients with the non AIDS-associated form of the disease but its use can be extrapolated to patients with all forms of Kaposi sarcoma.

Lo et al. (38) retrospectively reported on 60 patients treated with radiation therapy for Kaposi sarcoma, between 1954 and 1976, in order to assess treatment techniques and dose parameters. None of these patients had AIDS-associated Kaposi sarcoma as it was only described in 1981. Radiation

therapy technique used varied, with megavoltage electron therapy being used in 21 patients, supervoltage photon therapy in 12 patients and a combination of photons and electrons in 27 patients. The reported overall response rate was 93%. Complete responses occurred in 25 patients. In the presence of an adequate radiation dose, response to treatment was not significantly influenced by the treatment modality used. No significant complications were documented. The 3-year absolute survival rate was 57%. The study concluded that electrons or orthovoltage x-rays be used to treat small, localized lesions, that a combination of electrons and supervoltage photons be used to treat larger, infiltrative lesions and that total skin electrons with or without a photon boost be used for extensive disease. The results also suggested that a single dose of 8 – 12 Gy was adequate to treat localized lesions.

Nisce et al. (39) investigated the feasibility of using the technique of once weekly total (n=11) or subtotal (n=9) skin electron therapy to treat 20 patients with Kaposi sarcoma. It was not reported how many of these patients were diagnosed with AIDS-associated Kaposi sarcoma. The median follow-up was 48 months. The reported overall response rate was 100%. A complete response occurred in 85% and a partial response in 15%. No cases of early or late complications were reported. The results obtained in this group of patients was compared to results obtained in 20 patients who received treatment for individual lesions as required, a treatment technique termed the chasing technique. Disease recurred in 2 patients treated with the electron technique and in all

patients treated with the chasing technique. The authors concluded that the once weekly electron beam treatment technique was both successful in the management of extensive Kaposi sarcoma lesions and superior to the chasing technique with regard to long and short-term results.

Hamilton et al. (40) retrospectively analyzed 91 patients with Kaposi sarcoma, of which 3 patients had AIDS. The patients were treated with either local field radiation therapy (n=27) or extended field radiation therapy (n=56) in order to determine the effectiveness of the treatment in the management of this disease. In local field radiation therapy (LFR), orthovoltage x-rays of 100 – 250 KV were used and dose fractionation regimens varied from 3 Gy single fraction to 35 Gy in 5 fractions. Extended field radiation therapy (EFR) involved the treatment of at least half a limb with parallel opposed fields and megavoltage photon therapy to frequently prescribed doses of 8 Gy single fraction. Complete response occurred in 17 patients treated with LFR and in 38 patients treated with EFR. The actuarial relapse free survival was significantly different between the 2 groups, being better for the extended field treatment (p=0.04). Immunosuppression due to AIDS occurred in 3 of 12 patients and these patients were reported to have a similar treatment response to therapy when compared with the other patients in the study. The study concluded that radiation therapy is an effective treatment for Kaposi sarcoma and that extended field radiation therapy is preferred to local field radiation therapy in a patient with extensive disease.

MUCOSAL TOXICITY WITH IRRADIATION OF THE ORAL CAVITY AND OROPHARYNX:

Increased mucosal toxicity has been documented in patients treated to lesions of the oral mucosa with low doses of radiation.

Cooper and Fried (41) treated 4 patients with AIDS-associated Kaposi sarcoma of the oral cavity with radiation therapy and described increased toxicity from the treatment. All patients were male with an age range of 27 to 44 years. Radiation therapy technique involved the use of parallel-opposed lateral fields with ^{60}Co (n=3) and 4 MV photons (n=1) to field sizes ranging from 5.5 by 4.5 cm to 9 by 6.5 cm. Dose fractionation regimens prescribed were 30 Gy in 10 fractions (n=2), 30 Gy in 15 fractions (n=1) and 30 Gy in 20 fractions (n=1). All patients experienced treatment related toxicity before the total prescribed dose was reached. The first patient developed grade 3 toxicity halfway through the treatment. The second patient developed grade 1 toxicity at 18 Gy, which progressed to grade 3 toxicity by 27 Gy. The third patient developed grade 3 toxicity at 12 Gy. The fourth patient developed grade 2 toxicity at 7.5 Gy, which progressed to grade 3 toxicity over a period of 1 week. All cases of toxicity responded to conservative management. Local control of the primary Kaposi sarcoma lesion was maintained for the duration of follow-up (range: 3 – 7 months). The authors suggest that radiation therapy in the management of patients with AIDS-associated Kaposi sarcoma lesions of the oral cavity should be used as a last resort in view of the associated toxicity.

Watkins et al. (42) reviewed 12 patients with AIDS-associated oropharyngeal Kaposi sarcoma lesions treated with radiation therapy between 1982 and 1987 in order to describe their experience of increased mucosal toxicity and to put forward possible explanations. Radiation therapy was delivered in fractions of 1.5 - 3 Gy to total doses of 12 -18 Gy. With treatment doses of 12 Gy or more, 7 of 8 patients developed mucositis. In 4 of these cases the severity of the mucositis was serious enough to necessitate stopping treatment. In general however, mucositis was reported to occur 5 – 7 days after treatment, to progress over the next 3 – 5 days and then to resolve over the following 10 days. Factors such as, patient immune status, presence of oral candidiasis, use of systemic therapy and use of total body electrons in this study did not influence the incidence of mucositis. The authors concluded that patients with AIDS-associated Kaposi sarcoma receiving radiation therapy to the oral mucosa developed mucositis at lower doses of radiation and attributed this phenomenon to an altered ability to repair radiation damage in the oral mucosa in patients diagnosed with AIDS.

Kao et al. (43) retrospectively reviewed 8 HIV positive patients with lesions in the oral cavity and oropharynx treated with radiation therapy from 1 January 1994 to 31 December 1994. The histology of the lesion was Kaposi sarcoma in 4 patients and lymphoma or squamous cell cancer in the remaining 4 patients. The Kaposi sarcoma group was compared with the non-Kaposi sarcoma group in terms of treatment response and toxicity. The mean follow-up was 2.5 years. Patients with Kaposi sarcoma were irradiated to a treatment field of 568 cm^3 and a mean dose of 19 Gy while non-Kaposi sarcoma patients were treated to a field

size of 2636 cm^3 and a mean dose of 62.6 Gy. Mucositis occurred more frequently in patients with Kaposi sarcoma (p=0.1) as did weight loss, reported as 5.8 kg in Kaposi sarcoma patients versus 0.1 kg in non-Kaposi sarcoma patients (p=0.005). The study concluded that radiation therapy was an effective treatment for oral cavity and oropharyngeal tumours in HIV positive patients but patients with Kaposi sarcoma who received this treatment developed mucositis more frequently despite being treated to smaller fields with lower doses of radiation.

RADIATION THERAPY AT SPECIFIC SITES:

The thin elastic epidermis present in the ophthalmic area and genitalia may render these sites more susceptible to radiation toxicity and radiotherapy to these sites require special consideration.

Shuler et al. (44) retrospectively reviewed 12 patients with ophthalmic AIDS-associated Kaposi sarcoma lesions with radiation therapy in 1 of 3 studies, to determine treatment response. Radiation therapy was delivered according to a standard protocol of 20 – 30 Gy in 2 – 3 Gy fractions with 6 MV photons or 100 KV superficial x-rays according to the lesion characteristics. Complete response was reported in 10 patients. Local recurrence was documented in 2 cases after 4 months of follow-up. Toxicity of skin erythema (n=6) and hair loss (n=1) was reported. The authors concluded that radiation therapy in the management of ophthalmic Kaposi sarcoma lesions provides safe and effective palliation.

Ghabrial et al. (23) retrospectively reviewed 42 male patients treated with radiation therapy for AIDS-associated Kaposi sarcoma lesions of the conjunctiva or eyelids in order to describe treatment response. Between February 1984 and February 1991, 49 sites received either 8 Gy single fraction radiation therapy (n=31) or a variety of fractionated regimens to total doses of 15 – 36 Gy (n=18). Treatment response was assessed in 48 sites. The complete response rate was 32% and the partial response rate was 68% in patients treated with 8 Gy single fraction (Group 1). The complete response rate was 22% and the partial response rate was 72% in the group of patients treated with a variety of dose fractionation regimens (Group 2). Recurrence occurred in 22% of cases at a mean of 7.7 months in Group 1 and in 39% of cases at a mean of 6 months in Group 2. Only cases of minor toxicity were documented and were comparable between the 2 treatment groups. The study concluded that 8 Gy single fraction radiation therapy is safe and effective in the palliation of patients with AIDS-associated Kaposi sarcoma lesions of the conjunctiva and eyelids

Vapnek et al. (45) retrospectively reported on 19 male patients with AIDS-associated Kaposi sarcoma of the penis and scrotum treated with radiation therapy, between February 1985 and February 1990, in order to determine the effectiveness of the treatment as a palliative modality. The radiation therapy treatment technique used varied with lesion characteristics. Radiation was delivered in fractions of 1.5 – 8 Gy to total doses of 6 – 30 Gy. The most commonly used dose fractionation regimen was 8 Gy single fraction. The mean follow-up was 1 year. The overall objective response rate was 89%. A complete

response occurred in 33% of cases and a partial response in 56%. Recurrence was documented in 8 patients. Skin ulceration occurred in 1 patient. The authors concluded that radiation therapy in the management of AIDS-associated Kaposi sarcoma lesions of the male genitalia provide effective palliation.

Le Bourgeois et al. (17) described the outcome of radiation therapy in the management of 146 patients with epidemic Kaposi sarcoma at specific sites. Between January 1987 and December 1992, 186 lesions were treated in the oral cavity (n=35), ophthalmic area (n=102) and the male genitalia (n=49) with either 4 MV or 45 KV x-rays to a total dose range of 10 – 30 Gy according to lesion characteristics. The complete response rate in lesions of the oral cavity was 11% and the partial response rate was 89%. Toxicity occurred at low doses of 15 Gy and was reported as mild in 63%, moderate in 15% and severe in 22% of cases. Recurrences were documented in 6 instances at an average of 5.6 months. The complete response rate in ophthalmic lesions was 54% and the partial response rate was 42.1%. Toxicity was reported as mild in 77.5%, moderate in 19.6% and severe in 2.9% of cases. Local recurrences were documented in 12.8% at an average of 6 months. The complete response rate in genital lesions was reported as 69.4% and the partial response rate was 30.6%. Toxicity was reported as mild in 80%, moderate in 14% and severe in 6% of cases. Recurrence was documented in 45.4% at 3 months. The authors concluded that radiation therapy is an effective treatment for epidemic Kaposi sarcoma and recommended the use of doses of 15 Gy for oral lesions and 20 Gy for ophthalmic and genital lesions.

SUMMARY OF THE LITERATURE:

Most studies in the literature have shown that AIDS- associated Kaposi sarcoma is a radio responsive disease with reported response rates of greater than 85%. A dose response effect has been shown but despite the improved treatment response, local control and diminished residual pigmentation with increasing dose, a significant recurrence rate still occurs even at high total doses (16). There is no consensus on dose fractionation regimen in the literature. Longer fractionated regimens to total doses of 15 Gy for oral mucosal lesions, 20 Gy to sensitive sites such as the genitalia and eyes and 30 Gy to cutaneous lesions have been recommended (17, 18, 19). Many authors favour the 8 Gy single fraction regimen to achieve palliation in patients who have a limited life expectancy as the duration of response to the 8 Gy single fraction regimen is generally shorter than the longer dose fractionation regimens (16, 20, 21, 22, 23, 24). The 8 Gy single fraction regimen has also been shown to improve cosmesis for a limited duration of time (22).

Radiation therapy technique has not been extensively studied in patients with AIDS-associated Kaposi sarcoma but the treatment techniques employed in patients with non AIDS-associated Kaposi sarcoma can be utilized. Most authors individualize treatment modality and technique based on the patient's general medical condition, the symptoms present and the lesion characteristics of site, size and depth. Treatment modalities commonly used include electrons, orthovoltage x-rays and megavoltage photons. Localized radiation therapy fields

are used (36). However, some authors have reported better results with the use of extended radiation therapy fields for extensive disease (39, 40).

Radiation therapy for AIDS-associated Kaposi sarcoma is well tolerated with most studies reporting mild grade 1 or 2 toxicities. Significant toxicity of note was mucositis, which occurred at lower radiation therapy doses in patients receiving treatment to lesions of the oral cavity, which prompted a maximum radiation dose recommendation of 15 Gy to these sites (17, 18, 19). The feet were also noted to be more susceptible to radiation toxicity and care should therefore be taken when irradiating this site (20, 35). No serious toxicities were noted with radiation therapy to AIDS-associated Kaposi sarcoma lesions of the ophthalmic area or the male genitalia (23, 44, 45).