5. Discussion

Similar to other studies, mixed breed dogs, Labradors and Golden Retrievers were the most common breeds treated and Golden Retrievers were the most common breed with oral sarcoma (BREHM et al., 1995; BREWER, . and TURREL, 1982; CIEKOT et al., 1994; GRAVES et al., 1988; KUNTZ et al., 1997; MCKNIGHT et al., 2000; POSTORINO et al., 1988). The lack of data concerning demographics of the referral population prohibits conclusions concerning breed prevalence. As was the case in other reports, the relatively high median weight (32 kg) suggests an overrepresentation of large breed dogs (BREHM et al., 1995; BREWER and TURREL, 1982; CIEKOT et al., 1994; GRAVES et al., 1988; KUNTZ et al., 1997; MCKNIGHT et al., 2000; POSTORINO et al., 1988). The age distribution found in this study is consistent with other studies that have shown STS to be most common in middle to older aged dogs (BOSTOCK and DYE, 1980; FORREST et al., 2000; POSTORINO et al., 1988). Dogs averaged 8.7 years of age, the mean and median ages of dogs with HPC being greater than dogs with FSA; similar findings have been described in other reports (BOSTOCK and DYE, 1980). Studies limited to surgical treatment of STS such as KUNTZ et al (1997), and BOSTOCK and DYE (1980) reported an older treatment group (10.6 and 9.2 (FSA)-10 (HPC) years, respectively) than did this study where mean age was more consistent with other reports of surgery combined with radiation (FORREST et al., 2000; MCKNIGHT et al., 2000). The consistent discrepancy in age between dogs treated with surgery as a lone modality and multi-modality therapy may partially be explained by owner bias, as some owners may be reluctant to pursue radiation therapy in a geriatric dog.

As has been shown in other reports, HPC was more common in females than males (FORREST et al., 2000; GRAVES et al., 1988; MILLS and NIELSEN, 1967). In contrast to BREHM et al. (1995), MPNST was more common in female dogs. The vast majority of dogs were either spayed or neutered, however this likely reflects the reproductive status of dogs of the regional referral base. Like other studies of radiation treatment for soft-tissue sarcoma, the extremities were the most common anatomic location, with the distal extremity being more common than the proximal extremity (FORREST et al., 2000; MCKNIGHT et al., 2000). Studies restricted to the surgical treatment of STS such as KUNTZ et al. (1997) and

BOSTOCK and DYE (1980) describe common sites to be the proximal extremity and trunk, with the distal extremity being infrequent. Dissimilarities exist concerning the reporting of oral tumor locations. TODOROFF et al. (1979) described a greater frequency of occurrence in the maxillary region than in the mandibular region and sarcoma of the palate to be infrequent. BREWER and TURREL (1981) reported no mandibular tumors while THRALL (1980) reported more mandibular tumors than maxillary tumors. Mandibular tumors were absent in this study with maxillary tumors being most common. Consistent with CIEKOT (1992), all histological low-grade yet biologically high-grade fibrosarcoma were located in the maxilla.

Variation in the reporting of tumor location between studies concerning surgical treatment as a lone modality and studies of radiotherapy following incomplete excision is not surprising. Dogs usually receive radiation therapy after failing surgery or if surgery is not a viable option. The disparity in location between this study and KUNTZ et al. (1997) is likely a result of the differing inclusion criteria of the two studies. KUNTZ et al. (1997) included animals that received surgery as a lone modality and this study was limited to animals that received radiation, with the most common indication for RT being incomplete resection. The successful resection of STS requires a 2-3 cm margin of healthy tissue in all planes of dissection for complete excision to be achieved. The sparse connective tissue covering of the distal extremity, combined with the proximity of structures such a vessels, nerves and tendons that are abundant in the distal extremity present obstacles in obtaining adequate surgical margins that may result in a higher failure rate of surgery and an overrepresentation of the distal limb in the radiotherapy population. Dogs with mandibular tumors were generally referred for mandibulectomy, which may account for mandibular tumors not being represented in this study.

Few clinical studies of STS have incorporated multiple histotypes. Fibrosarcoma was the most prevalent tumor type in this study, followed by HPC, MPNST and Misc tumors. Other studies have described HPC (BOSTOCK and DYE, 1980; FORREST et al., 2000) as being more common than FSA, or MPNST to be most common and HPC infrequent (KUNTZ et al., 1997). Variation between studies may be due to differing criteria of animals entering the studies, or in differences classifying STS between pathologists. The radiation treatment population is largely defined by referral. Differences in the referral process between institutions may also be responsible for the disparity of reported tumor type frequencies. Alternatives to marginal excision followed by RT include repeated excision or radical resection. Differences exist between surgeons concerning the criteria considered relevant for forming a treatment plan (e.g. type, grade, location); different courses of action may be taken according to tumor criteria. Some surgeons may prefer ablative surgeries for some histotypes or locations that may reduce or eliminate their inclusion in the radiation treatment group studied.

The lack of consensus between this study and studies involving surgery as a mainstay of treatment on the frequency of tumor type, anatomic site and age suggests that dogs receiving radiation treatment for STS are not representative for the general STS population. Caution is advised when applying results concerning presentation or patient demographics from this study to the general STS population.

Twenty-eight tumors went ungraded in this study. The majority of tumors that were not graded were HPC, which have been reported to be somewhat less aggressive, less likely to metastasize and more radio-controllable than other tumors in the STS family (BOSTOCK and DYE, 1980; MCCHESNEY et al., 1989b). Referral pathology was often not sought when the initial report did not describe a morphological appearance consistent with aggressive biological behavior. Other tumors were not graded because of their unique character, such as lymphangiosarcoma or infiltrative lipoma where insufficient data exists concerning grading. Some tumors were described in equivocal terms such as “low-to intermediate-grade”; while such a grade does not formally exist, it is of adequate clinical utility to conduct treatment without seeking a referral pathology opinion. Tumors were more consistently graded after 1997, following clinical reports of the prognostic implications of tumor grading. The disparity in follow-up between tumor types is reason to be suspicious of results generated in this study concerning the prognostic relationship of intermediate-grade sarcoma to low or high-grade sarcomas.

The survival event in this study was defined as death due to loss of local tumor control, the development of metastasis or radiation toxicity. Of the dogs that died of tumor related causes in this study, 12/17 dogs died as a result of local tumor invasion, 3/17 died from metastasis, and 2/17 developed fatal radiation toxicity. Two aspects of local tumor control, the development of recurrence and measurable disease were found to negatively correlate with survival, as was oral location.

Few studies exist that concern the use of radiation in the treatment of incompletely excised STS of the oral cavity. As described in a report restricted to excised sarcoma (FORREST et al., 2000), non-oral tumors had a survival advantage over oral tumors. In this study, 17 dogs were treated for oral sarcoma. Fourteen dogs received a definitive protocol, nine had undergone resection prior to irradiation and five dogs were treated for measurable oral disease. Three dogs were treated with a palliative protocol for oral sarcoma. In contrast to FORREST et al. (2000), oral location was a negative prognostic factor for local recurrence (p=0.0175), four of nine tumors returned (44%) compared to seven of 51 non-oral tumors (14%). One reason for reduced survivability of oral sarcoma was the difficulty incurred during excision of recurrent tumors; complete excision of recurrent oral disease was rarely successful. Four of nine recurrent non-oral tumors were cleanly re-excised compared to one of four cases of recurrent oral sarcoma. In contrast to dogs in Group I, the development of recurrence in Group II was more closely associated with death. Three of four recurrent tumors in the oral cavity resulted in death, compared to two of seven non-oral recurrences. The less successful excision of oral STS compared to non-oral STS following radiation failure is not surprising as the difficulty of excising oral lesions is well documented (BOSTOCK and DYE, 1980; KOSOVSKY et al., 1991; KUNTZ et al., 1997; SCHWARZ et al., 1991a; SCHWARZ et al., 1991b).

Five of fourteen dogs that received a definitive protocol for oral sarcoma were not candidates for surgery prior to irradiation; all five dogs died of tumor related causes. Median survival was 226 days with 2/5 surviving over one year. Similar results were achieved by THRALL (1980) where median survival was 6.4 months after completing radiation therapy. Longer survival times have been achieved in other studies. Studies that have examined the treatment of measurable disease have had rigid exclusion criteria such as limitations on invasion which may have excluded more advanced or aggressive disease (THEON et al., 1997b). Other studies made no mention of the indication for treating measurable disease with radiation; in some studies it was a primary treatment modality. In this study, radiation was used as a therapeutic modality when surgery was not possible. Tumors that are not amenable to resection must be viewed as prognostically unfavorable, which may have contributed to the discrepancy in survival between studies.

Several studies have shown that measurable soft-tissue sarcomas exhibit a limited clinical response to radiation treatment (MCCHESNEY et al., 1989b; THRALL, 1981; THRALL et al., 1996). Studies that incorporate surgical resection prior to radiation have consistently shown superior local control and survival (FORREST et al., 2000; MCKNIGHT et al., 2000). However, no randomized studies have directly compared radiation vs. radiation in combination with surgery, so it is difficult to quantify the advantage that cytoreduction imparts. In this study, patients who received the benefit of surgery prior to radiation showed superior survival and local control over dogs that were treated for measurable disease. In addition to the five oral sarcomas that received radiation treatment, three dogs with non-oral sarcoma received definitive treatment for visible disease. One dog was still alive 949 days after receiving definitive radiotherapy for an infiltrative lipoma; similar success has been described in a larger series of infiltrative lipomas (MCENTEE et al., 2000). Another dog died survived 748 days after treatment for hemangiopericytoma invading the caudal thigh; this case was consistent with the 33% two-year survival rate described in MCCHENSEY et al. (1989). Radiobiological principles predict that the addition of surgery offers an increased clonagen growth fraction and alleviation of tumor hypoxia with improved clonagen radiosensitivity accompanied by superior survival and local control (LARUE and GILLETTE, 1996; MCLEOD and THRALL, 1989; THRALL, 1997). However, it should also be considered that patients that received radiation in the face of measurable disease were not candidates for marginal excision due to advanced disease or an anatomic location that prohibited resection, which may have contributed to inferior survival of dogs with measurable disease. The design of this study does not allow for a direct comparison between radiation vs. radiation and cytoreduction, but it can be concluded that tumors that are not amenable to excision carry a worse prognosis than excisable tumors.

Three dogs in this study died of STS metastasis, in two dogs metastatic lesions were confirmed to be of spindle-cell origin. One of the hallmarks of STS is a low rate of metastasis (MACEWEN and WITHROW, 1996; MAULDIN, 1997; WITHROW, 1998b). In this study, the metastatic rate was 4.5% in dogs treated with a definitive radiation protocol, which is lower than has been reported in other studies. FORREST et al. (2000) reported metastasis in five of 35 dogs (14%). KUNTZ et al. (1997) reported a 17% metastatic rate (41% in high-grade sarcoma) in dogs treated with surgery. MCKNIGHT et al. (2000) reported an 8% metastatic rate in dogs that received RT and surgery for the treatment of non-oral sarcoma. The large number of HPCs in this study may have contributed to the low metastatic rate; no dog with HPC developed metastasis. The rarity of HPC metastasis has been documented in other studies such as GRAVES et al. (1988) (0%, n=23), EVANS (1988) (0%, n=20) and BOSTOCK and DYE (1980) (1.2 %, n=86). In contrast to FORREST et al. (2000), MCKNIGHT et al. (2000), and KUNTZ et al. (1997) doxorubicin was offered for high-grade sarcoma. The addition of chemotherapy to the treatment protocol may have contributed to the lower rate of metastasis in this study over other studies. None of the dogs that received doxorubicin developed metastasis although they belonged to a higher risk population (higher grade tumor) than did dogs that did not receive doxorubicin. However, two dogs with high-grade tumors that were not treated with doxorubicin developed metastasis. Although such findings are not to be weighted heavily, they are consistent with recommendations concerning the use of adjuvant chemotherapy (MAULDIN, 1997; PAGE and THRALL, 2000). Metastasis may have been missed in some dogs as necropsies were not performed and dogs that are still alive may develop metastasis. One dog with a liposarcoma developed metastasis in the abdominal cavity. The biological and metastatic behavior of liposarcoma lacks reports containing a large number of cases and has eluded comprehensive description. In contrast to other STS that usually metastasize to the lung, several small series have described metastasis to the abdomen in dogs with liposarcoma as was the case in this study (DAVIS et al., 1974; SAIK et al., 1987; STRAFUSS and BOZARTH, 1973). An expanded role of abdominal sonography in assessing and monitoring dogs with liposarcoma may be appropriate.

In human medicine, tumor grade has been shown to be an important predictor of survival (COLLIN et al., 1988; HEISE et al., 1986; STOJADINOVIC et al., 2001a; STOJADINOVIC et al., 2002b). Dissimilar to other studies concerning radiation in combination with surgery in dogs (FORREST et al., 2000; MCKNIGHT et al., 2000), grade was found to be prognostic for survival in dogs with incompletely excised non-oral sarcoma (Group I). In contrast to MCKNIGHT et al. (2000) that contained no high-grade tumors, this study contained six high-grade non-oral tumors. The survival of dogs with Grade I tumors was statistically different from Grade II and Grade III tumors in this study. Two dogs with Grade III tumors died of metastatic disease and two dogs with Grade II tumors died of local recurrence. No dogs with ungraded tumors or Grade I tumors died to sarcoma related disease. All recurrent low-grade and ungraded tumors were cleanly re-excised or re-irradiated and stabilized. Studies involving the surgical treatment of STS have shown that grade and mitotic index influence survival with high-grade tumors fairing worse (BOSTOCK and DYE, 1980; KUNTZ et al., 1997). Kuntz et al. had a 41% metastatic rate with high-grade tumors. This was higher than the incidence of metastasis in this study, which was 33% in dogs with high-grade non-oral sarcoma.

Histotype, location, grade, interval between surgery and radiation therapy, field-size and surgical history were examined as factors that influence the DFI of irradiated, incompletely excised, non-oral soft-tissue sarcomas.

An association between tumor type and local tumor control has not been demonstrated in dogs that have received radiation therapy for STS, although one report from human medicine detected an inferior prognosis for MPNST. In this study, five of seven recurrences were MPNST and an inferior DFI was noted compared to HPC or FSA. Two of the five MPNST recurrences were accompanied by unusual circumstances. One low- grade MPNST that returned as a high-grade undifferentiated sarcoma 1,197 days after the completion of radiation therapy was likely a radiation induced neoplasia. An early recurrence (77 days post RT) outside of the RT field was associated with a surgical report inconsistent with current surgical recommendations (WITHROW, 1998c) and represented the shortest recurrence interval in Group I. Malignant peripheral nerve sheath tumor was the most common tumor type represented in MCKNIGHT et al. (2000), but in contrast to this study MPNST was not associated with a poor prognosis. In the study conducted by MCKNIGHT et al. (2000), all recurrences were noted outside the boundaries of the radiation field. In this study, five non-oral tumors recurred inside the boundaries of the radiation and two tumors recurred were out side the radiation field. Recurrences inside the boundaries of the radiation field represent tumors that received radiation and were not controlled with the dose delivered whereas out of field recurrences represent disease that escaped radiation delivery. In MCKNIGHT et al. (2000), 63 Gy was delivered as a standard treatment dose compared to 52.5 Gy used in this study. Higher doses have been associated with superior control of HPC and FSA, but no data concerning the dose response of MPNST has been reported. It cannot be excluded that the reason for the higher rate of return of MPNST is due to a difference in dose response between HPC, FSA and MPNST at the dose used in this study. Additional progressive studies examining the dose response relationship in canine MPNST would be of utility. Aggressive dose delivery for MPNST may be appropriate.

In human medicine, location is prognostic for achieving local control (HEISE et al., 1986; TOROSIAN et al., 1988), with distal extremity lesions being more responsive to treatment than central locations. In this study, a low P-value was found in DFI between tumors of the head/neck and distal extremity; this result should not be over interpreted as only three tumors of the head/neck were included, one returned after 580 days and two were censored after short intervals. Twenty-five tumors of the distal extremity were treated and only two recurred (4%). The distal extremity appeared to show superior control compared to more centrally located tumors, however a statistical difference was not clearly demonstrated. Success achieved in the distal extremity may possibly result from the higher prevalence of tumor types such as HPC that have been shown to be more radioresponsive than other histotypes (MCCHESNEY et al., 1989b). One distal extremity tumor recurrence that occurred inside the radiation field almost five years after treatment is more likely a result of vital clonagen surviving radiation than failure to irradiate residual tumor cells. The sparse soft-tissue covering of the distal limb may limit distortion of the surgical field away from the surgical scar and allow for radiation to be delivered more accurately to subcutaneous layers with superior targeting of residual disease. In human medicine, amputation has largely been replaced by limb sparing surgery in combination with radiation (CATTON et al., 1996; CATTON et al., 1999; PARSONS et al., 2001). The success achieved in controlling tumors of the distal extremity with RT is of clinical importance, as curative surgery often requires amputation for tumors of the distal limb (BOSTOCK and DYE, 1980; BREHM et al., 1995; KUNTZ et al., 1997). The excellent long-term prognosis offered by marginal excision followed by RT may condense the practice of amputation for STS in dogs.

Surgical history was examined as a factor of local recurrence. A history of multiple surgeries was not associated with inferior DFI. It is, however, interesting to note that all dogs that underwent multiple surgical procedures prior to receiving radiation treatment showed recurrence earlier than any dog that was treated after a single surgery. In contrast to MCKNIGHT et al. (2000), six of seven non-oral tumors recurred in dogs where surgery was conducted by a referral surgeon; all eight recurrences in MCKNIGHT et al. (2000) were in dogs that received surgery prior to referral.

A delay between surgery and radiation treatment was not found to be of prognostic importance in this study, although delay has been associated with increased morbidity and mortality in humans (SCHWARTZ et al., 2002). Although no difference was detected, exceptionally long delay cannot be recommended, as recurrence prior to initiating RT is a possibility. The statistical methods examined the dependency of DFI on the delay between surgery and radiation therapy, not the converse. Conclusions concerning the independence of the surgery to radiation interval on recurrence are inappropriate. An extended delay may allow for tumor cells to multiply and approach radiobiological behavior of measurable sarcomas, although little is know about the radioresponsiveness of canine sarcoma during the transition from residual disease to measurable disease. Of the dogs that were treated for macroscopic disease, several had undergone previous resection that did not seek immediate referral and presented only after recurrence when surgery was no longer possible. The median delay between surgery and radiation therapy was longer than in other reports (EVANS, 1987; FORREST et al., 2000; MCKNIGHT et al., 2000), as all surgeries were conducted at other facilities and a delay was incurred in the referral process.

Dissimilar to EVANS (1987) and reports from human medicine (FEIN et al., 1995; FREW et al., 1995; HEISE et al., 1986; SPUNT et al., 1999; STOJADINOVIC et al., 2001a; WOLFSON et al., 1998), but similar to other reports (FORREST et al., 2000), field size (as an estimation of tumor size) was not shown to be predictive for local recurrence. Dogs that showed recurrence did not have large mean field sizes, and the recurrence rate was not higher in dogs with field-sizes over 75 cm^2. Dogs that received treatment with electrons were excluded from analysis because the area eliminated by the use of custom blocks was not consistently reported. As a result, tumors of the thorax were preferentially eliminated from analysis of field-size and recurrence. The resulting decrease of the amount of available data decreases the sensitivity of detecting a relationship between field-size and DFI. The findings in the study are dissimilar to EVANS (1987) where dogs with portal size under 50 cm^2 had longer tumor free intervals than dogs with portals greater than 50 cm^2. Although fewer animals were included in EVANS (1987), the total number of recurrences was higher than in this study. The lack of recurrence in this study makes detection of a difference more difficult. Dogs in EVANS (1987) were treated with orthovoltage radiation. Megavoltage radiation offers superior dose distribution compared to orthovoltage radiation, especially with larger field sizes and may also explain the different findings between studies.

Two recurrences in Group I occurred in dogs treated with electron beam radiation and tumor control was lost in five dogs that were treated with photon beam radiation. Superiority of one radiotherapeutic modality over the other in achieving tumor control was not apparent. Although not apparent from survival analysis, electrons were a useful modality in this study. The availability of electron therapy expanded the spectrum of patients that could be treated safely. One patient with a history of multiple excisions for a STS of the lumbar region was referred from a distant institution that was not equipped with electron capacity and had concerns about the patient’s safety if treatment were to be undertaken with photon therapy. Additional patients that received electron treatments may not have received treatment due to toxicity concerns if photon therapy was the only available treatment option.

The results presented here show that a favorable disease free interval can be reached in non-oral STS without amputation or extensive surgery. In this study, 86% of dogs with non-oral tumors that underwent resection were alive after three years, and 84% were disease free at three-years. KUNTZ et al. (1997) described an 85% long-term control rate in non-oral STS when treated with aggressive surgery alone, which is similar to the 84% three year control rate demonstrated in this study. Although similar local control was achieved with surgery, it is difficult to meaningfully compare the results presented here with the results described in KUNTZ et al. (1997).

The patients in this study were all treated for non-resectable disease or incomplete resection, both of which represent the limitations of surgery as a treatment modality. KUNTZ et al. (1997) described cases treated only with surgery and excluded patients that received adjuvant chemotherapy or radiotherapy. As radiation treatment is indicated for incomplete resection, surgical failures were likely treated with radiation and excluded from the study. Comparison of aggressive surgery vs. surgery with adjuvant radiation treatment is limited by the lack of parameters available for comparing the two treatment modalities. Quality of life issues do not lend themselves to convenient objective comparisons. Several studies that have focused on surgical treatment have required limb amputation (BREHM et al., 1995; GRAVES et al., 1988; KUNTZ et al., 1997), which is an obvious disadvantage that may not be reflected in survival analysis. In this study, amputation was not undertaken in any dog, although it may have been of benefit in selected cases. Radiation may be suited for some owners who would otherwise pursue euthanasia instead of radical surgery or in dogs where orthopedic issues prohibit limb amputation. Radiation therapy involves repeated treatments, which represent a commitment in time and financial resources on the part of the owner. Radical resection is generally less expensive and less time consuming and may be a more appropriate option for some owners.

Radiation therapy was generally well tolerated in this study. Repeated anesthesia was uneventful in all dogs that received radiation; no dog died or suffered serious anesthesia related morbidity. Similar to other studies, acute radiation toxicity was not dose limiting (FORREST et al., 2000; MCKNIGHT et al., 2000). Although acute effects such as dry and moist desquamation were seen in almost all animals, resolution was generally not problematic. Major radiation reactions did occur in a limited number of dogs and included secondary tumors of the radiation field. As was the case in other studies, two dogs developed osteosarcoma in the radiation field (MCCHESNEY et al., 1989b; MCKNIGHT et al., 2000; THRALL et al., 1981; THRALL, 1984). One dog developed OSA shortly after receiving a second course of radiation for a recurrent tumor that was treated previously at another institution. Another dog developed OSA of the palate after enjoying a long tumor free interval. Even though the cause of death in this dog was radiation related, a long disease free interval was experienced. Oral FSA offers a poor prognosis; surgical intervention offers a mean survival of approximately one year (KOSOVSKY et al., 1991; WALLACE et al., 1992). Despite the severity of the radiation reaction, survival was more likely prolonged by radiation than shortened. A third dog developed a high-grade anaplastic sarcoma in the treatment field of a tumor that was originally excised as a low-grade MPNST.

Although tumor return with a loss of differentiation is possible, the difference in morphology between the original tumor and the recurrent tumor suggests a radiation induced sarcoma, as described elsewhere (THRALL, 1984).

Palliative radiation, in a strict sense, is delivered with the goal of pain relief and an improvement in the quality of life without the aim of increasing survival. Guidelines for the use of palliative radiation in human medicine have been adapted to veterinary radiation oncology and suggest that palliative radiation not be given when a definitive protocol may be curative (SIEGEL and CRONIN, 1997; THRALL and LARUE, 1995). As definitive radiotherapy is unlikely to offer long-term control for measurable soft-tissue sarcoma and the stabilizing effect of hypo-fractionated radiation on STS is unknown, difficulty is encountered in rigidly applying guidelines concerning palliative radiation to macroscopic sarcoma.

Six dogs received hypofractionated radiation as a sole treatment modality in this study. Five dogs were treated for measurable sarcoma and one dog with significant co-morbidity was treated for residual disease. Four of the five dogs that received palliative RT as a sole radiotherapeutic modality for measurable disease responded to treatment; either pain control or improved function was noted. Similar results have been achieved for the treatment of osteosarcoma (RAMIREZ et al., 1999). As has been shown in other studies of hypofractionated radiation (BATEMAN et al., 1994b; BLACKWOOD and DOBSON, 1996; BREARLEY, 2000), treatment was well-tolerated and no dog suffered major radiation toxicity. The study of dogs that received palliative radiation is somewhat limited by the difficulty in accurately assessing a radiation response. A measurable tumor response was neither expected nor a premise of treatment; however there does appear to be a stabilizing effect, as tumor shrinkage was noted in several dogs.

Complications of re-irradiation have been reported to correlate with short intervals between radiation treatments. Control rates with definitive courses of radiation have been reported to result in long term control in 38% of all cases, with an estimated complication rate of 12% (TURREL and THEON, 1988). One dog in this study received two full courses of radiation in this study. Although the period between treatments was five-years, catastrophic toxicity occurred in the form of an extraosseous OSA occurring in the treatment field. In two other cases, re-irradiation involved the use of a palliative protocol to a total dose approaching 7000 cGy. The use of a palliative protocol as a second course of radiation has received little attention in veterinary medicine. Although higher total doses are associated with increased risk of late reactions, most do not manifest until 6-12 months after radiation delivery. In this study neither dog that was re-irradiated using a hypofractionated protocol developed major toxicity. Hypofractionated re-irradiation may be a viable option in dogs with recurrent disease in dogs with limited expected survival.