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Objective—To determine results of intracranial meningioma resection by use of a surgical aspirator and assess prognostic factors associated with intracranial meningiomas in dogs.

Design—Retrospective case series.

Animals—17 dogs.

Procedures—Medical records of dogs that underwent resection of an intracranial meningioma by use of a surgical aspirator were reviewed. Information pertaining to signalment, imaging findings, clinical signs, duration of clinical signs, preoperative treatment, location of the tumor, results of histologic assessment, outcome, and necropsy results was obtained from the medical record. Clients and referring veterinarians were contacted via telephone for information on recurrence of clinical signs and postoperative survival time.

Results—16 dogs were >7 years of age, and all 17 dogs had seizures before surgery. The most commonly affected breed was the Golden Retriever, represented by 6 of the 17 dogs. Median survival time was 1,254 days. Of the data collected, only histologic subtype of the tumor was prognostic. Analysis of survival times according to histologic tumor subtypes indicated that the order from most brief to longest was as follows: anaplastic, 0 days; fibroblastic, 10 days; psammomatous, >313 days; meningothelial, >923 days; and transitional, 1,254 days.

Conclusions and Clinical Relevance—Use of a surgical aspirator to resect intracranial meningiomas in dogs was associated with longer survival times than those achieved with traditional surgery alone or traditional surgery combined with radiation therapy. Dogs with meningothelial, psammomatous, or transitional intracranial meningioma subtypes appeared to have a better prognosis than dogs with other subtypes of meningioma. (J Am Vet Med Assoc 2006;229:394–400)

Abbreviations

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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<td>CT</td>
<td>Computed tomography</td>
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<td>KBr</td>
<td>Potassium bromide</td>
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<td>WHO</td>
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Intracranial neoplasia has a reported incidence of 14.5 cases/100,000 dogs.1 Meningiomas are the most commonly reported primary intracranial tumor in dogs,2 and the most common anatomic locations are the frontal lobe, falx cerebri, and cerebellopontine angle.2 The configuration of the tumor’s attachment to the dura or leptomeninges may be narrow (pedunculated), broad (sessile), or total (meningioma en plaque).3 Therapeutic goals for treatment of canine intracranial meningiomas include complete excision or cytoreduction of the tumor and control of secondary effects. Clinical treatment modalities that are presently available for veterinary patients include medical management, surgery, chemotherapy, and radiation therapy. Medical treatment is primarily palliative and includes administration of glucocorticoids, anticonvulsants, or both. Mean survival times reported for dogs that received palliative treatment alone ranged from 59 to 81 days in 1 study.4 Surgical excision alone resulted in median survival times of 6 to 7 months in other studies.5,6 At present, no chemotherapeutic agent is considered to have definitive activity against intracranial meningiomas in humans,7 although results of 1 study indicate that hydroxyurea may be useful for treatment of unresectable or recurrent meningioma. Megavoltage radiation therapy yielded a mean survival time of 7.5 months when used alone in 16 dogs and a median survival time of 16.3 months when used in conjunction with surgical excision in 13 dogs.5 This finding was similar to findings reported in humans, in which the cause-specific survival rate at 15 years was greater in patients treated with total excision or subtotal excision followed by radiation therapy, compared with those treated with subtotal excision alone.

If surgery is to be performed, total excision is always the surgical goal, although this is not always attainable.8 Complete excision of an intracranial meningioma may be difficult because of anatomic location, absence of a clear demarcation between affected and healthy brain tissue, tumor infiltration into healthy brain parenchyma, and tumor friability. Because of these factors, complete excision has been attempted with various surgical devices to assist the surgeon in achieving complete excision while minimizing hemorrhage and destruction of unaffected brain parenchyma. One such device is the surgical aspirator. A surgical aspirator is a device that enables the surgeon to ablate tissue high in water content (eg, tumor tissue or organ parenchyma) while sparing tissue that is low in water content.9,10 The use of a surgical aspirator is especially useful when surgical margins are close to critical structures,11 such as the brainstem,12 optic apparatus,13 or cranial nerves.14 One of the earliest and most widely used surgical aspirators was the aspiration cup, a device that was developed in the early 1900s.15 Although this device was simple and effective, it was limited in its ability to remove large amounts of tissue.16

To overcome this limitation, the surgical aspirator was developed.17 The surgical aspirator is a device that enables the surgeon to remove large amounts of tissue quickly and efficiently.18 The device consists of a probe that is inserted into the tumor and attached to a vacuum source.19 When the vacuum is turned on, the probe creates a suction effect that pulls tissue into the aspirator.20 The aspirator then removes the tissue and deposits it in a collection chamber.21 The suction effect allows the device to reach areas that are difficult to access with a surgical blade.22 The aspirator is particularly useful for removing tissue that is adherent to the brainstem, optic apparatus, or cranial nerves.23 The suction effect also helps to minimize hemorrhage and trauma to surrounding structures.24

The surgical aspirator is a safe and effective device that can be used to assist in the resection of intracranial meningiomas.25 Its use can improve surgical outcomes by allowing for complete excision of the tumor with minimal trauma to surrounding structures.26 For this reason, the surgical aspirator should be considered as an adjunct to traditional surgical techniques in the treatment of intracranial meningiomas.
in water content (eg, vessel walls).{11,12} Surgical aspirators have a tip that vibrates at various frequencies and fragments tissue while simultaneously lavaging and aspirating material from the surgical field. This results in less hemorrhage and enhanced surgeon ability to view the surgical site, which enables more extensive removal of tissue with a higher margin of safety in highly vascular or anatomically sensitive regions.{11,12}

Surgical aspirators have been used in veterinary medicine in subtotal or partial prostatectomies,{11,12} for location of intrahepatic shunts,{15} and for resection of intracranial masses,{11,12} and other soft tissue tumors. Applications for surgical aspirators in human medicine are numerous and include use in transphenoidal hypophysectomy for pituitary lesions,{16} resection of hepatic parenchymal lesions,{17} and resection of intracranial meningiomas.{1} Potential complications associated with use of surgical aspirators include damaging healthy brain parenchyma at higher power settings{8} and aerosolization of viable neoplastic cells.{19}

Resection of an intracranial meningioma with a surgical aspirator has been reported in a single instance in the veterinary literature, to the authors' knowledge. The purpose of the present study was to evaluate a series of dogs in which resection of intracranial meningioma was performed by use of a surgical aspirator.

**Criteria for Selection of Cases**

Medical records of dogs examined at The Animal Medical Center from 1999 to 2004 were retrospectively reviewed. All dogs with a diagnosis of intracranial meningioma and in which the tumor was removed via a surgical aspirator were considered for the study.

**Procedures**

**Preoperative evaluation**—Diagnosis of an intracranial mass was made via MRI or CT in all dogs. Information pertaining to age, sex, breed, CT or MRI findings, preoperative clinical signs, duration of clinical signs, preoperative treatment, and anatomic location of the tumor was collected from the medical record. Metastatic disease was ruled out on the basis of findings on thoracic radiographs and results of a CBC, serum biochemical analysis, and abdominal ultrasonographic imaging.

**Surgical technique**—Anesthetic protocols were similar for all dogs. Dogs were premedicated with an opioid (hydromorphone [0.05 to 0.1 mg/kg [0.02 to 0.05 mg/lb], IM], methadone [0.3 mg/kg [0.14 mg/lb], IM], or oxymorphone [0.05 mg/kg, IM]) and an anticholinergic drug (atropine [0.02 mg/kg [0.01 mg/lb], IM] or glycopyrrolate [0.01 mg/kg [0.005 mg/lb], IM]). Methylenidamfinosolone sodium succinate was administered IV at the beginning of the surgical procedure at a dose of 30 mg/kg (13.6 mg/lb), and a second dose of 15 mg/kg (6.8 mg/lb) was administered IV 2 hours later.{20} Anesthesia was induced with propofol (3 mg/kg [1.4 mg/lb], IV), diazepam (0.5 mg/kg [0.2 mg/lb], IV), and fentanyl (3 µg/kg [2.3 µg/lb], IV). Dogs were intubated and provided with 100% oxygen via an open circle system into which a mechanical ventilator was incorporated.

Anesthesia was maintained via continuous IV infusion of fentanyl and propofol initially (at rates of 0.7 µg/kg/min [0.32 µg/lb/min] and 0.4 mg/kg/h [0.2 mg/lb/h], respectively), with adjustments in rate made on the basis of anesthetic depth. Mechanical ventilation was used in all dogs with a goal of maintaining PaCO2 at 30 to 32 mm Hg.{21} Parenchymal swelling observed intraoperatively was assumed to be cerebral edema and was controlled with administration of mannitol (0.25 g/kg [0.11 g/lb], IV) and furosemide (2 mg/kg [0.9 mg/lb], IV), as needed.

The surgical technique was similar in all dogs. A transfrontal or rostrotentorial surgical approach was performed in each instance, depending on the anatomic location of the tumor. For the transfrontal craniotomy technique, a bone flap was created by use of an oscillating sagittal saw. Bone tunnels were pre-drilled for wiring of the bone flap. The cribriform plate was removed by use of a high-speed burr and Rongeur forceps. For the rostrotentorial approach, craniectomy was performed by use of a high-speed burr and Rongeur forceps. A durotomy was performed, and all grossly visible tumor was removed by use of a surgical aspirator{1} with a 36-kHz handpiece (Figures 1 and 2). Starting settings were as follows: amplitude, 100%; aspiration, 30%; irrigation, 3 mL/min; and a power setting of 3+. Settings were adjusted during surgery depending on the texture of the tumor tissue. All associated dura or falx cerebri was sharply resected if possible, and multiple sections of tumor were submitted for histologic analysis. Hemorrhage was controlled via placement of hemostatic clips, bipolar electrocautery, and application of hemostatic sponges{8} when appropriate. All durotomy incisions were left open. In dogs that underwent transfrontal craniotomy, the bone flap was replaced and secured with 24-gauge orthopedic wire. The bone flap was not replaced in dogs that underwent the rostrotentorial approach. Soft tissues were closed routinely. Dogs were weaned off the ventilator in a routine manner and recovered from anesthesia in the intensive care unit. While in recovery, dogs were positioned with the head above the level of the heart until alert and responsive and were observed for seizure activity, decreased mentation, or hypoventilation.

**Postoperative evaluation**—Information pertaining to postoperative complications, histopathologic diagnosis, length of hospital stay, postoperative treatment, recurrence of clinical signs, postoperative survival time, and necropsy results was obtained from the medical records. If not available in the medical records, information was obtained from the referring veterinarian or client via telephone conversation.

**Statistical analysis**—Median survival time was calculated by use of the Kaplan-Meier product limit method{23} with commercially available statistical analysis software.{8} Because of the limited number of cases evaluated, appropriate nonparametric statistical testing (eg, Mann-Whitney U test, Spearman rank correlation, and χ² with Fisher exact test) was used. All recorded variables (age, sex, neuter status, breed, treatment type, tumor location, and tumor histologic subtype)
were evaluated for their effect on survival time by use of Kaplan-Meier life table analysis, log-rank testing, and Cox proportional hazards analysis, when appropriate. Dogs were censored if they were lost to follow-up or died because of disease other than intracranial meningioma. All recorded variables were evaluated for potential associations. Differences were considered significant when the P value for a 2-tailed test was ≤ 0.05.

Results

Signalment and preoperative evaluation—Diagnosis of meningioma was confirmed via histologic evaluation in all dogs, and slides were reviewed by a single pathologist (SM). Twenty dogs met the inclusion criteria, but 3 were excluded from the study because they were lost to follow-up immediately after discharge from the hospital. Of the 17 dogs included in the study, 6 were male and 11 were female. Of the males, 4 were neutered. Of the females, all 11 dogs were neutered. Median age was 10 years (mean, 9.6 years; range, 6 to 12 years). The Golden Retriever was the most common breed represented (6/17), followed by the Labrador Retriever (4/17). Breeds represented by 1 dog each were Yorkshire Terrier, Boxer, Bullmastiff, American Staffordshire Terrier, Miniature Poodle, Springer Spaniel, and mixed breed. All dogs had had seizures before surgery. In addition to seizures, 1 of the dogs had circling episodes, 1 had Horner’s syndrome, and 1 had a head tilt. Preoperative treatments administered included phenobarbital and dexamethasone (n = 7); phenobarbital alone (4); KBr alone (1); phenobarbital, KBr, and prednisone (1); phenobarbital and prednisone (2); phenobarbital, dexamethasone, and KBr (1); and KBr and dexamethasone (1). Duration of preoperative clinical signs ranged from 4 to 240 days (median, 60 days; mean, 76.5 days). Anatomic locations of the tumors were characterized on the basis of MRI or CT findings as prefrontal (n = 6), caudal cerebral or cerebellar (1), associated with the olfactory bulbs (3), parafalcine (4), frontoparietal (1), ventrolateral thalamus (1), and temporal (1). Approaches used included the transfrontal (n = 12) and rostroventral (5) approaches. For the 1 dog with a meningioma of the caudal portion of the cerebrum and the cerebellum that was deemed unresectable, a rostroventral approach that extended dorsally and caudally to the region of the nuchal crest was used.

Postoperative outcome—Postoperative complications included mild epistaxis (n = 1), aclinical bradycardia (1), hyperthermia (1), decreased mentation and nonambulatory tetraparesis (1), death (1), persistent obtundation (1), status epilepticus (1), left-sided hemiparesis (1), and pneumoencephalus (1). Fourteen of the 17 dogs were discharged from the hospital. Of the dogs that did not survive to hospital discharge, one was euthanatized intraoperatively because of an unresectable mass, one died 2 days after surgery in the hospital, and one was euthanatized 10 days after surgery because of persistent obtundation. One dog died of status epilepticus 27 days after surgery. Mean hospitalization time for dogs that survived to discharge from the hospital was 4.3 days (range, 2 to 22 days). Postoperative treatment included phenobarbital (n = 1); prednisone and KBr (2); prednisone and aspirin (1); phenobarbital and prednisone (4); phenobarbital and aspirin (2); phenobarbital and dexamethasone (1); phenobarbital, methylprednisolone sodium succinate, mannitol, and aspirin (1); phenobarbital and methylprednisolone sodium succinate (1); mannitol, KBr, methylprednisolone sodium succinate, and diazepam (1); and phenobarbital, methylprednisolone sodium succinate, and prednisone (1).

Histologic results—Tumors were classified according to the WHO classification scheme for meningiomas. The meningioma was classified as anaplastic in 1 of the
17 dogs, fibroblastic in 1 dog, psammomatous in 3 dogs, meningothelial in 6 dogs, and transitional in 6 dogs.

**Necropsy data**—Necropsy was performed in 3 dogs. In the dog that died 27 days after surgery in status epilepticus, necropsy findings included severe meningoencephalitis and cerebral arteriole thrombosis but no evidence of residual meningioma tissue. One dog died 225 days after surgery; necropsy in that dog revealed a mast cell tumor in the inguinal area; thyroid carcinoma; and histiocytic sarcoma in the lung, mediastinum, liver, kidneys, and muscle of the left thoracic limb. No regrowth of meningioma was evident. Another dog died 387 days after surgery with recurrence of neurologic signs; in that dog, necropsy revealed meningioma regrowth in the region of the pituitary gland adjacent to the previous surgical site.

**Long-term outcome**—Median survival time was 1,254 days (Figure 3). No variables were found to be prognostic via log-rank analysis or Cox proportional hazards analysis. No biologically important associations were found. Comparison of survival times on the basis of histopathologic tumor subtypes revealed median survival times (as determined by Kaplan-Meier analysis) as follows: anaplastic tumors, 0 days; fibroblastic tumors, 10 days; psammomatous tumors, >313 days (median not reached); meningothelial tumors, >523 days (median not reached); and transitional tumors, 1,254 days (P = 0.004).

When dogs with transitional and meningothelial histologic tumor types were combined as a group and compared on the basis of survival times with dogs in the psammomatous-other group, dogs in the transitional-meningothelial group had a median survival time of 27 days (P = 0.023; Figure 4). With Cox proportional hazards analysis, the hazard ratio for the psammomatous-other group (ie, the likelihood of dying from that type of tumor vs from a transitional-meningothelial tumor) was 13.69, with a 95% confidence interval of 1.453 to 125.0 (P = 0.022).

Because dogs with anaplastic and fibroblastic subtypes of tumors did so poorly in relation to dogs with other histologic subtypes of tumors, data for anaplastic and fibroblastic tumors were combined and compared with data from all of the other histologic tumor types combined. Dogs in the anaplastic-fibroblastic group had a median survival time of 10 days, whereas dogs in the meningothelial-psammomatous-transitional group had a median survival time of 1,254 days (P = 0.002; Figure 5).

No postoperative radiation therapy was used in any of the dogs. Two dogs received chemotherapy in the form of hydroxyurea administered at a dosage of 50 mg/kg (23 mg/lb) 3 times/wk on days 499 and 1,405 after surgery. Hydroxyurea treatment was initiated in those dogs because of MRI findings that were suggestive of tumor recurrence. Clients were offered radiation therapy for the dogs but declined that option. The end point for calculation of survival times in those 2 dogs was the point at which treatment with hydroxyurea was initiated to prevent influence from confounding factors. Both dogs were alive at the time of writing and had survived for 999 and 1,523 days after surgery, with a mean survival time of 1,262 days (42.1 months).
Discussion

Clinical signs associated with intracranial meningiomas are varied and depend on the location of the tumor, tumor size, and rate of growth. Seizures are the most commonly reported clinical sign in dogs. All 17 of the dogs in the present study had seizures as a clinical sign. It has been reported that dolichocephalic breeds and Golden Retrievers may be at increased risk for developing intracranial meningiomas, and most tumors are detected in dogs > 7 years old. Sixteen of the 17 dogs in the present study were 7 years of age or older, and the most common breed affected was the Golden Retriever (6/17). No sex predilection for the tumor has been reported in dogs. Meningiomas are the most common benign intracranial neoplasia in humans and are usually detected in middle-aged females. Female dogs were slightly overrepresented (11/17) in our study. It has been reported that from 18% to 27% of meningiomas are malignant, and pulmonary metastasis has been reported in 3 dogs. No evidence of metastasis was found in any of the dogs in the present study.

Median survival time for dogs in this study was 1,254 days, a value that exceeded survival times in dogs managed with standard surgical excision alone or in conjunction with radiation therapy. We believe that use of a surgical aspirator allows the surgeon to perform a more complete or aggressive tumor resection, thereby possibly resulting in fewer incomplete resections. We speculate that the longer survival times reported in the present study were attributable to these benefits. The use of surgical aspirators decreases intraoperative mortality and recurrence rates that are associated with intracranial meningioma resection in humans, and our results were consistent with those findings. In the present study, 3 of 17 dogs died in the perioperative period before being discharged from the hospital. One of those dogs had an anaplastic meningioma that was deemed unresectable at the time of surgery and was euthanatized during surgery. Of the 2 dogs that died in the hospital after surgery, 1 had severe cerebral swelling and hemorrhage during surgery.

Of the variables analyzed in this study (age, sex, breed, treatment type, tumor location, and tumor histologic subtype), only tumor histologic subtype was found to have prognostic value. Median survival times for anaplastic, fibroblastic, psammomatous, meningothelial, and transitional tumor subtypes were 0, 10, > 313, > 523, and 1,254 days, respectively. Survival times were also different when transitional and meningothelial types of tumors were grouped together and compared with the psammomatous-other group. From those data, it appears that dogs with meningothelial, psammomatous, and transitional tumor subtypes have a much better prognosis, compared with dogs that have tumors of the anaplastic and fibroblastic subtypes.

In humans, meningiomas are categorized histologically as grade I, II, and III on the basis of the WHO classification scheme. Grade I meningiomas include psammomatous, transitional, meningothelial, and fibroblastic subtypes. Grade II meningiomas include atypical and chordoid subtypes. Grade III meningiomas include anaplastic and papillary subtypes and are considered to be the most aggressive. The WHO classification of meningiomas in domestic animals does not include categorization of subtypes into different grades. A list of patterns common to human and veterinary patients includes meningothelial (meningotheliomatous), fibrous, transitional, psammomatous, angiomatous, papillary, and anaplastic tumors.

Our results with the anaplastic meningioma subtype mirror findings in humans with intracranial meningiomas, in which WHO grades II (atypical) and III (anaplastic) tumors are associated with a poor clinical outcome. This is probably a result of increased local aggressiveness and proliferation of those subtypes of tumors, thereby decreasing the likelihood of complete removal. The poor outcome observed in dogs that had the fibroblastic meningioma subtype was inconsistent with characteristics reported in humans, in which the fibroblastic subtype is classified as grade I meningioma and has a more favorable prognosis. However, because only a single dog with fibroblastic meningioma was included in the present study, meaningful conclusions cannot be made about the behavior of this subtype of meningioma in dogs.

To the authors’ knowledge, there are no previous studies relating prognosis to meningioma subtypes in veterinary species. This information could be valuable in postoperative and preoperative client counseling, but preoperative tissue diagnosis is rarely obtained for intracranial lesions in dogs. However, use of a modified CT-guided stereotactic brain biopsy system in dogs has been reported as a rapid, accurate means of tumor biopsy with a low complication rate and may be more widely utilized in the future. If preoperative tissue biopsy specimens are obtained more routinely, determination of prognostic factors such as histologic subtype may be helpful in choosing the best treatment.

The recurrence rate of intracranial meningiomas in humans is 9% to 12% with grossly complete excision and may be as high as 40% with incomplete excision. There are many factors that may be evaluated to determine the likelihood of recurrence of an intracranial meningioma. For example, recurrence of meningioma in humans in which excision was grossly complete has been correlated with tumor shapes characterized as mushroomed or lobulated. In addition, the risk of recurrence has been associated with tumor location, histologic features, resection type, and tumor growth in adjacent nervous tissue. Regrowth of tumor even with complete resection is thought to result from the presence of meningothelial tumor cells in adjacent nervous tissue or thickened arachnoid membrane. Many molecular markers are being studied to further elucidate risk factors for recurrence. A high proportion of progesterone receptors in meningiomas in the CNS in dogs and cats has been reported, but recurrence rates were not examined in that study and the prognostic usefulness of the information is undetermined. In another study in dogs with incompletely resected meningiomas treated with megavoltage radiation therapy, the progression-free survival rate was higher with tumors that had a low (ie, < 24%) proliferating cell
nuclear antigen index. Recurrence was confirmed in only 1 dog in the present study but was thought to be likely in 2 other dogs that had recurrence of neurologic signs and follow-up MRI findings consistent with tumor regrowth. Treatment with hydroxyurea was initiated in the dogs at 499 and 1,405 days after surgery; both dogs were alive at the conclusion of this study (at 909 and 1,525 days after surgery, respectively).

Hydroxyurea is an antimetabolite drug that inhibits synthesis of nucleic acids. In humans, use of hydroxyurea for treatment of intracranial meningiomas has been described as ineffectual delaying progression of the disease, and potentially resulting in full remission with long-term treatment. To the authors' knowledge, no studies in which the benefits of hydroxyurea treatment were proven in dogs with intracranial meningiomas have been published, but initial results are encouraging enough to consider evaluation in clinical trials in the future.

Disadvantages associated with the use of a surgical aspirator include high initial cost, steep learning curve, the potential for damaging normal brain parenchyma (particularly at higher power settings), aerosolization of viable tumor cells, and the need for experienced technical staff for setup and maintenance of the device. It has yet to be determined what combination of treatment modalities (surgery, radiation, and chemotherapy) and order of their application will result in the longest survival times.

Results indicated that use of a surgical aspirator to resect intracranial meningiomas in dogs was associated with better survival times than are achieved with traditional surgery alone or traditional surgery combined with radiation therapy. An unexpected finding was that dogs with meningothelial, psammomatous, or transitional intracranial meningioma subtypes appear to have a better prognosis than dogs with other meningioma subtypes. Further studies are needed to investigate the effects of adding hydroxyurea, radiation therapy, or both to the treatment plan of dogs undergoing resection of intracranial meningiomas with a surgical aspirator. In addition, further studies are needed to investigate whether the prognostic correlation between histopathologic classification and outcome is valid and could be used to determine the need for adjuvant treatments.


d. Statview, SAS Institute Inc, Cary, NC.

References


