A Comparison of Radiography Versus Computed Tomography in the Diagnosis of Middle Ear Disease in the Dog

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A COMPARISON OF RADIOGRAPHY VERSUS COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF MIDDLE EAR DISEASE IN THE DOG

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ABSTRACT

The purpose of this study was to compare CT and radiography for diagnosing the presence and severity of middle ear disease in dogs with chronic otitis externa. Thirty-one dogs that were presented for a total ear canal ablation and bulla osteotomy were recruited. Three normal dogs served as controls. All dogs were examined using radiography and CT. Three radiologists independently evaluated imaging studies in random order. A visual analog scale method was used for scoring certainty and severity of middle ear disease. Surgical findings were recorded intra-operatively. Bulla lining samples were submitted for histopathology and scored by a single pathologist who also used a visual analog scale system. Findings from both modalities agreed more closely with surgical findings than with histopathology findings. With either surgery or histopathology as the gold standard, CT was more sensitive than and as specific as radiographs for predicting presence and severity of middle ear disease. Overall severity of middle ear disease was lower in the right versus the left ears. For CT, inter-observer variance of middle ear certainty was 217.04 while radiographic variance was 126.14 on the side with lower severity estimates. Both radiography and CT were more accurate for predicting the severity of the disease than its presence. Findings indicate that CT is more accurate and reliable than radiography in diagnosing middle ear disease for dogs with chronic otitis externa, but only when severity of disease is moderate or high. With low severity of disease, reader diagnostic certainty for both modalities becomes more variable.

DEDICATION

This project is dedicated to my parents- Joe and Judy, who always believed in me and made it possible for me to follow my dreams, to my siblings Jay and Jan and their family, for their support and love, and to my cats-Squeakers and Willie, who were always there for me when I needed them.

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CHAPTER 1
LITERATURE REVIEW

Anatomy of the canine middle ear

The middle ear consists of an air-filled tympanic bulla, a short canal leading to the nasopharynx (auditory or eustachian tube), and the tympanic membrane.[1] A layer of epithelium and lamina propria line the tympanic cavity. A part of the tympanic bulla cavity is covered by a simple squamous epithelium and the remainder is lined with ciliated columnar epithelium. The columnar epithelium starts near the auditory tube and is continuous with the epithelium of the auditory canal and the nasopharynx. The cilia on the epithelial cells constantly move a layer of mucus down the eustachian tube and into the nasal cavity. The auditory tube permits equalization of air pressure between middle ear and the outside atmosphere. [2] The tympanic membrane covers the entrance of the tympanic cavity and separates the middle ear cavity from the external auditory meatus. [1] The tympanic membrane is divided into two parts: the pars flaccida and the pars tensa. The pars flaccida extends dorsally from the lateral process of the malleus to the tympanic notch, forming the upper quadrant of the tympanic membrane. [3] The pars tensa is the remainder of the membrane and is a thin, tough connective tissue layer consisting of outer radial and inner circular fibers. [4] The dorsal aspect of the middle ear cavity houses three auditory ossicles: the malleus, incus and stapes, with their associated muscles. These three small bones transmit air vibrations from the tympanic membrane, across the middle ear to the inner ear via the vestibular or oval window. [1] Amplification of sound waves is provided by the leverage of the ossicles and by the greater surface area of the tympanic membrane, which transmits sound waves to the smaller surface area of the vestibular window. [2] The two skeletal muscles, the tensor tympani and the stapedius, damp excessively loud noises. [2] Multiple nerves pass through the middle ear, but only the

facial and sympathetic nerves appear to be clinically significant. [3] The facial nerve exits the brainstem along with the vestibulocochlear nerve and passes the medial aspect of the bulla in the facial canal. This canal opens into the cavity of the middle ear near the vestibular window. [1] The sympathetic nerve leaves the cranial cervical ganglion, located just behind the tympanic bulla, and enters the middle ear cavity.

Etiology of middle ear disease

Otitis Media can be primary or secondary to other disease processes. Primary otitis media is uncommon. [3] Primary secretory otitis media of Cavalier King Charles Spaniels may be due to increased production of viscous mucus, decreased drainage of the middle ear by the eustachian tube, or a combination of the two. [5] Secretory otitis media can also be caused by ciliary dysfunction. [6] This is often the case with primary ciliary dyskinesia. In humans it has been established that people afflicted with otitis media with effusion (OME) have abnormal transportation of mucus from the middle ear and the number of secretory cells and glands is substantially increased. [5]

Secondary otitis media can be initiated through many routes. The most common of these routes in dogs is extension of inflammation across the tympanic membrane from primary otitis externa. In one study of 100 dogs diagnosed with otitis externa, 16% of the acute cases and 52% of the chronic cases had concurrent otitis media at surgery. [7] Extension of inflammation through the auditory canal is another potential cause of otitis media. Cats may develop otitis media through this route as a sequela to upper respiratory tract disease. [8] One study of 7 dogs and one cat describes secondary middle ear disease associated with congenital palatine defects. [9] Inflammation through this pathway is likely linked to ascending infections or malfunction of the eustachian tube preventing adequate drainage of the tympanic bulla. Otitis media may also be the secondary result of hematogenous spread of an infection but it rarely occurs. [10]

Neoplasia, inflammatory polyps, migrating foreign bodies, and trauma can also affect the middle ear of dogs. Neoplasia originating within the middle ear of dogs is rare. [11] In a study of neoplasia involving the middle ear cavity of dogs, a majority of neoplastic processes arose in the external auditory meatus. [11] The only neoplasm to originate within the middle ear cavity was papillary adenoma. Neoplastic invasion of the tympanic bulla is also attributed to squamous papilloma, ceruminous gland adenocarcinoma, basal cell tumor, sebaceous gland adenocarcinoma and an anaplastic carcinoma. [11] [12] [13] [14] [15] Squamous cell carcinoma could originate in or invade the middle ear of dogs and cats. [16] [17] [18] A report describes a neoplasm of the middle ear causing vestibular syndrome in a dog. [19] Reports of nasopharyngeal or aural inflammatory polyps in dogs are uncommon. [20] However, inflammatory polyps are more common in the cat[21]. Most polyps originate from the mucosa of the tympanic cavity or eustachian tube. From this location, polyps may extend either to the external ear canal or nasopharynx or both. [22] [20] In a report on five dogs with inflammatory polyps, all t polyps originated within or immediately adjacent to the tympanic cavity and extended into the external ear canal. The author suggested that inflammatory polyps were associated with otitis externa and media. [20] In cats, chronic bacterial infections, ascending infections from the nasopharynx, viral infection, and congenital causes all have been suggested as potential etiologies. [10] [20] Because of the variable location of the polyp, clinical signs can include respiratory stridor, dyspnea, dysphagia, and signs of external or middle ear disease. [23]

Aural choleasteatoma has been reported as a form of an epidermal cyst found within the middle ear cavity of dogs. [24] True cholesteatoma is an erosive expanding lesion in which hyperkeratotic epidermis is confined within the middle ear cavity. [25] In one study of inflammatory ear disease in the dog, aural cholesteatoma was found to accompany otitis media in seven of sixty-two ears examined. [24] These lesions resembled cholesteatoma in humans where it is an important and irreversible complication of chronic otitis media. [24] Cholesteatoma can complicate otitis media by promoting bone

resorption and by causing bone erosion. If bone erosion is severe, t neurological abnormalities and life threatening intracranial complications can occur. Cholesteatoma formation should be differentiated from uncomplicated otitis media and neoplasia involving the middle ear of dogs. [24] It is thought that cholesteatomas in dogs form from a pocket of tympanic membrane which becomes adherent to the inflamed middle ear mucosa. [24] Other pathogenesis theories include congenital origins, metaplasia of the respiratory epithelium, and immigration of stratified squamous epithelium from the external ear or tympanic membrane. The prognosis for dogs in which cholesteatoma accompanies otitis media appears to be poorer than for those in which cholesteatoma is absent. [26]

Another serious complication to otitis media is otitis interna. The most common route of infection of the inner ear is most likely otitis media secondary to otitis externa. [27] Failure to effectively resolve otitis media may result in extension of infection to the inner ear. [28] Various exotoxins, as well as endotoxins from *Haemophilus influenza* and *E. coli* can traverse the round window membrane that separates the middle ear from the inner ear. [29] In addition, inflammatory mediators produced in the middle ear cavity following otitis media may be responsible for cochlear dysfunction. [30] The clinical signs of otitis interna include asymmetric ataxia; head tilt, circling to the side of the lesion, horizontal or rotatory nystagmus and positional or vestibular strabismus. [23] If osteomyelitis of the osseous bulla and petrous temporal bone occurs then there may be extension of infection from the middle and inner ear to the central nervous system resulting in brain stem abscess, meningitis, or meningoencephalitis. Spread of infection from the middle and inner ear to the brain may occur by erosion through the medial aspect of the petrous temporal bone, by migration of bacteria along existing vascular or neuronal pathways, or via hematogenous spread. [31] Early clinical signs of intracranial involvement may be difficult to recognize. Abnormalities that may indicate central nervous system involvement include depressed mentation, proprioceptive deficits, paresis or multiple

cranial nerve deficits. [31] Intracranial extension of infection causing mengioencephalitis and brain abscess has a poor prognosis when the condition is not recognized early and treated aggressively.

Pathophysiology of otitis media

Otitis media is a disease process characterized by inflammation of the middle ear cavity. [25] Otitis media has been documented in species such as cats, pigs, tigers, dogs, cattle and humans. [23, 32-34] Inflammation may originate at the middle ear or is extension from other disease processes.[3] The most common source of inflammation in the canine middle ear is extension from the external ear.[27] The middle ear defense mechanisms include a mucociliary system and a cellular and humoral defense system. [23].The function of the mucociliary system is to clear foreign material and prevent ascending infections. The cellular and humoral defense mechanisms include the use of secretory products and the initiation of inflammation by inflammatory mediators. Secretory products include lysozymes secretion by the epithelial cells and collagen and ground substance by fibroblasts. They help form a mechanical barrier to protect against the spread of microorganisms. [3] Inflammatory mediators initiate an inflammatory stage of otitis media that is characterized by a morphological change occurring in the lamina propria of the middle ear mucosa. These changes include dilation and increased permeability of capillaries, edema of the lamina propria, and leukocyte infiltration. In the acute phase, the infiltrate consists primarily of polymorphonuclear leukocytes and macrophages. Macrophages are phagocytic and presumably play a helper role in the induction of an immune response by processing and presenting antigen to B and T lymphocytes [3] Any fluid accumulation is usually serous and is believed to be primarily a blood serum derivative that enters the extracellular spaces owing to increased permeability of the subepithelial vessels. With further progression of the disease, metaplasia of the middle ear epithelium occurs with proliferation of goblet cells and mucus glands. [35] Additionally,

there may be a reduction in the number of ciliated cells necessary to clear the mucus. These changes are characteristic of the late acute to subacute stages of otitis media. It is during this time that mucosal effusions most often become evident. [25] In the chronic stages of otitis media, alterations of the middle ear structures become more apparent. Several of the inflammatory mediators and growth factors produced by activated mononuclear cells are important in the development and proliferation of granulation tissue. [25] Granulation tissue that has direct contact to bone often is associated with focal inflammation and bone resorption. The bone resorption occurs due to the formation of osteoclasts from mononuclear macrophages within the granulation tissue as well as the production of substances with osteolytic properties. [36] Mineral opacities, termed otoliths, have also been detected within the middle ear of dogs with radiography and computed tomography. [37] Otolithiasis may represent mineralized material of a current or previous case of otitis media. [37]

Patients with otitis media generally have signs of otitis externa. [23] These include discharge from the external ear canal, pawing or rubbing the affected ear, shaking the head, or pain when the head is touched. [23] Signs of facial nerve involvement may be seen and include drooping of the ear or lip on the ipsilateral side, increased salivation, decreased or absent palpebral reflex and exposure keratitis. Horner's syndrome may occur secondary to damage of the sympathetic nerve as it passes through the middle ear. Ptosis, miosis, enopthalmos, and protrusion of the nictitating membrane are the clinical signs seen with Horner's syndrome. [3] If otitis media is chronic and severe enough to cause otitis interna, signs of abnormal vestibular function may develop. [23] These clinical signs of otitis interna include head tilt, nystagmus, and ataxia. Motor deficits to the limbs and other cranial nerve abnormalities may be seen if the disease process reaches the meninges through the internal acoustic meatus.

Treatment of middle ear disease

The essential treatment in most cases of otitis media consists of eliminating the infected, inflammatory or foreign material from the bulla and providing drainage for discharge. [3] Medical management is usually attempted and results evaluated before surgical procedures are performed. Assessing the degree of chronicity, the results of otoscopic examination, and changes seen with diagnostic imaging are determinants of the likelihood of successful medical therapy. Otoscopic exam is usually used to assess the changes to the external ear epithelium and to evaluate the status of the tympanic membrane. Changes seen with diagnostic imaging modalities include increased opacity within the bulla cavity, lysis or proliferation of the bulla wall or change in the bulla contour. The more chronic cases with severe soft tissue and bony changes will have less successful therapeutic outcomes if managed medically. Systemic antibiotic therapy is recommended in those cases that do not have otoscopic or radiographic evidence of fluid or material within the middle ear cavity. [27] The choice of antibiotics should be based on results of culture and susceptibility testing. [28] In cases in which cultures cannot be obtained, broad-spectrum antibiotics should be selected. Typically, long-term (4-6 weeks) systemic antibiotic therapy yields the best results. Broad-spectrum antibiotics such as aminoglycosides should not be administered on a long term basis because of ototoxicity. If little or no improvement is observed after antibiotic therapy for 4-6 weeks, reassessment is indicated. [3,27] Organisms cultured most frequently from infected middle ears in decreasing order of frequency include *Pseudomonas* sp., *Staphylococcus intermedius*, *Malassezia*, beta hemolytic *Streptococcus*, *Cornebacterium*, *Enterococcus* species, *Proteus* species, *E.coli* and anaerobic bacteria. [10] In cases in which *Pseudomonas* spp. is cultured and is resistant to gentamycin, adding a solution that increases the permeability of the cell wall may enhance the susceptibility of the bacteria to the antibiotic. This can be accomplished with a lavage solution containing

ethylenediamineetetraacetate (EDTA), tromethamide, or TRIS (2-amino-2 [hydromethyl]-1,3-propanediol and lysozyme. [3] Depending on the size of the ear canal, 1-3 mls of solution can be instilled with gentamycin otic drops 2 or3 times a day. This treatment should be continued a minimum of two to three weeks. [3] If otitis externa and otitis media are present, the animal may benefit from the use of a topical preparation. Most otic preparations are a combination of antibiotics, anti-inflammatory agents and antifungal agents. Oral glucocorticoids may also be considered to reduce canal swelling and facilitate irrigation. [10] In humans, there is some evidence that NSAIDS may decrease otalgia associated with acute otitis media. However, there has been no proof documenting that NSAIDS reduce or prevent inflammatory changes in the middle ear associated with acute otitis media or otitis media with effusion (OME). [38] The use of transtympanic tubes as a means of achieving drainage of the middle ear has been reported in the dog. [39] Complications from medical management of otitis media are few. The most common complication is failure of therapy or recurrence following withdrawal of antibiotic therapy. Infection may extend to the inner ear, resulting in vestibular signs. [27] Ototoxicity may result from the use of topical preparations containing aminoglycosides, chloramphenicol, iodine, and chlorhexidine that are inadvertently introduced into the middle ear through a perforation in the tympanic membrane. [27]

The most common indications for performing middle ear surgery are otitis media that has been refractory to less invasive methods, and chronic otitis externa that is complicated by hypertrophied soft tissues and presumed concurrent otitis media. [40] The status of the external ear canals, the diagnostic imaging appearance of the tympanic bullae, the microbiologic status of the middle ear, and the dog's ability to hear should be considered before surgery is performed.

One surgical approach used for the treatment of otitis media is a myringotomy or surgical incision of the tympanic membrane. A myringotomy is performed under anesthesia by perforating the caudoventral aspect of the pars tensa with a spinal needle

using an otoscope as a guide. After the incision, a specimen is collected for microbiologic sampling as well as cytological exam. [41] Flushing with 0.5 to 1 mL of sterile saline may be necessary if samples are not readily retrievable. [10] After the samples are obtained, the middle ear is flushed with a warm saline solution. The therapeutic objectives of a myringotomy are to reduce pressure in the middle ear, provide drainage of infected material, and allow instillation of medication to the middle ear cavity. [42] [40] When the otitis media is resolved, the myringotomy site will heal by second intention in about half of the animals. [43]

Numerous other surgical techniques are used for treatment of the otitis media, but only two provide adequate exposure and drainage of the tympanic cavity: lateral bulla osteotomy and ventral bulla osteotomy. [23] Combining a middle ear procedure with a procedure to treat otitis externa is the most appropriate treatment of the patient with severe, nonresponsive otitis externa and otitis media.

The lateral bulla osteotomy is typically performed with other external ear canal procedures. However, when it is performed by itself, the patient is placed in lateral recumbency with the affected side up. A skin incision is made over the vertical ear canal and extended 1-2 cm ventral to the horizontal canal. [23] Blunt dissection of the subcutaneous tissues allows the junction between the parotid salivary gland and the ventral aspect of the horizontal ear canal to be revealed. The facial nerve can be exposed by further dissection along the ventral and caudolateral aspect of the horizontal ear canal. The facial nerve should be retracted ventrocaudally near its exit from the stylomastoid foramen to expose the lateral aspect of the bulla. [41] The tissue overlying the bulla is incised with a scalpel blade and if necessary elevated with a periosteal elevator. [23] The bulla is then entered ventral to the horizontal ear canal with a Steinman pin or pneumatic drill. It is important to direct the pin or drill caudolaterally to avoid the auditory bones and structures of the inner ear. The osteotomy site is enlarged ventrally with a rongeurs to allow adequate visualization and access to the tympanic cavity. Microbiologic culture

and sensitivity testing should be performed of bulla contents. After cultures are obtained, the middle ear is irrigated with a warm sterile physiological saline solution and the bulla is curetted to remove debris and tympanic bulla lining. [40] The placement of a drain is chosen only if the bulla cannot be cleaned out adequately or extensive drainage is expected postoperatively. [44] The combination of lateral bulla osteotomy and total ear canal ablation (TECA) is used most commonly in animals with chronic proliferative otitis externa accompanied by otitis media. [41] The ear canal ablation is performed first to allow exposure of the external acoustic meatus, which will be used as the starting point of the bulla osteotomy. After the reflection of soft tissue from the lateral aspect of the tympanic bulla, rongeurs or a drill is used to enlarge the ventral aspect of the external acoustic meatus. The entire ventral aspect of the bony auditory meatus is removed and extended ventrally to allow visualization into the tympanic cavity and to allow proper drainage. The cavity is flushed and carefully curetted as described previously. [40] Aggressive dorsomedial curettage is not recommended as this may damage the vestibular apparatus. Once again a fenestrated drain may be placed to facilitate drainage. The drain is secured to the skin and routine closure of subcutaneous tissue and skin is performed. Ingress-egress drainage is rarely indicated and drainage of the surgical site is controversial. Lateral bulla osteotomy can also be combined with lateral ear resection or vertical canal ablation. Such combinations may be indicated in patients with otitis media and recurrent otitis externa with either minimal proliferative changes of the ear canal or changes limited to the vertical ear canal. [40] The performance of these combinations is infrequent.

The outcome of lateral bulla osteotomy in combination with other procedures on the external ear canal especially total ear canal ablation (TECA) has been favorable. In one study in which long term results of 26 dogs with TECA and lateral bulla osteotomy were known, 15 dogs (58%) had excellent results, and an additional 8 (31%) saw improvement in clinical signs. [45] Another study of the same procedures reported resolution in 97% of the surgically treated ears of dogs with chronic otitis externa and

media. [46] Serious postoperative complications such as neurologic deficits, vestibular injury, or persistent infection may occur following TECA. [44] Post operative complications as high as 40% have been reported. [45] Complications associated with peri-operative infection include prolonged incisional drainage, surgical wound dehiscence, and paraaural fistulation. [45] Resolution of fistulas that develop post-operatively by ventral bulla osteotomy suggests incomplete removal of the external ear canal and/or bulla lining. [45] Other infections or inflammation may resolve with the use of antimicrobial drugs and hot packing of the wound. [46] Poor surgical technique resulting in facial nerve trauma, abnormal anatomy, and scar tissue causing adhesions may all contribute to neurologic complications such as facial nerve paralysis. Intra-operative hemorrhage was a fatal complication reported in one study. [45] Long term results are described as excellent after TECA if the ear canal and all secretory tissue are excised completely, meticulous technique is used when exposing and retracting the facial nerve and curetting the tympanic cavity, and primary skin disorders are managed appropriately after surgery. [44, 45, 47] Another study comparing passive wound drainage to primary closure of total ear canal ablation- lateral bulla osteotomy (TECA-LBO) showed that primary closure is an acceptable alternative in dogs undergoing TECA-LBO when surgical wound dead space can be managed with meticulous hemostasis, complete debridement of devitalized tissue and accurate apposition of tissue planes. [48]

Another approach to the tympanic cavity is the ventral bulla osteotomy. Advantages of the ventral bulla osteotomy compared to the lateral bulla osteotomy include better visualization of the tympanic cavity, more consistent drainage of the middle ear cavity, ability to achieve bilateral exposure of the tympanic bulla without repositioning and reduced risk of injury to the facial nerve. [40] The disadvantage of performing this approach along with an external ear canal procedure is that the animal has to be repositioned. Therefore this approach is more commonly used in animals with minimal or no external ear disease. The procedure is performed by placing the patient in

dorsal recumbency. A paramedian skin incision is made just medial to the mandibular salivary gland and centered midway between the level of the angular process of the mandible and the level of the wings of the atlas. [40] The platysma muscle will need to be incised longitudinally along the skin incision. Blunt dissection is used to separate the digastricus muscle from the hypoglossal and styloglossal muscle. [23] Identifying the hypoglossal nerve on the lateral aspect of the hypoglossal muscle help verify the proper plane of dissection. [40] The hypoglossal nerve, hypoglossal and styloglossal muscles are retracted medially and the digastricus muscle laterally to identify the tympanic bulla as a raised rounded structure between the jugular processes caudally and the angular process of the mandible rostrally. Additional blunt dissection and reflection of muscle will be needed to facilitate exposure of the ventral bulla. The ventral aspect of the tympanic bulla is penetrated with a Steinman pin or a pneumatic drill. [23] The dorsal aspect of the tympanic cavity should be avoided. Rongeurs are used to enlarge the osteotomy site until good visualization of the middle ear cavity is achieved. [40] Once good visualization is achieved, microbial, cytological or histopathological samples should be taken. The cavity is then flushed with a warm saline solution, an antibiotic solution or appropriate antiseptic. [40] The middle ear cavity should be curetted to remove the remaining lining or inflammatory debris. An ingress-egress drain tube may be placed to facilitate drainage. The tube should enter and exit through separate ventral cervical skin incisions. The management of the drain is as described for the lateral bulla osteotomy. The subcutaneous tissue and skin are closed in a traditional fashion.

Outcome results following the ventral bulla osteotomy procedure alone for otitis media have been described as excellent in 90% of cases. [49] Another study describing ventral bulla osteotomy and a TECA on 13 dogs showed resolution of disease in 85% of cases after one surgery. The most common postoperative complications are similar to the lateral bulla osteotomy and TECA combination and include deafness, facial or hypoglossal nerve paralysis and recurrence of disease. [50] Deafness is attributed to

mechanical impingement of proliferative bone on the ossicular chain and tympanic membrane following surgery. [51] Facial nerve and hypoglossal nerve paralysis as well as damage to the parasympathetic nerve supply are possible neurologic complications, and may occur with or without a TECA. Recurrence of disease was similar to the lateral approach and is commonly due to remnants of ear canal integument or middle ear lining that remains following surgery. [50] [47] There have been no valid comparisons between lateral and ventral bulla osteotomy. Only a well-designed prospective study can accurately compare the two bulla approaches combined with ear canal ablation as a treatment for otitis externa and media. [50] Currently, both the lateral and ventral bulla osteotomy procedures are considered to be acceptable.

The same medical and surgical therapies used to treat otitis media are employed to treat other causes of middle ear disease. With neoplasia of the middle ear, surgical treatment alone is often unrewarding because of the anatomic location and local invasiveness. [23] Adjunctive radiation therapy or chemotherapy may be necessary for long-term remission. The treatment of choice for inflammatory polyps involving the middle ear is surgical excision. Treatment of otitis interna and mengioencephalitis usually entails aggressive medical and/or surgical management. Treatment should begin by correcting the underlying otitis media. Myringotomy or osteotomy is usually necessary. Long-term systemic antibiotics can be administered based on culture and sensitivity when possible. Empirical therapy should be chosen to provide a broad spectrum of coverage using bactericidal antibiotics with good blood brain barrier penetration. [31] Some intracranial lesions may require surgical exploration and drainage along with medical management to completely resolve the infection. If the infectious process is identified early and treated with appropriate antibiotics and/or surgery, the prognosis for recovery is good. [27] Residual vestibular deficits will likely be permanent.

Diagnostic imaging of the middle ear

Diagnostic imaging plays an important role in establishing a diagnosis of otitis media. Otoscopic examination of the middle ear is typically not possible due to an intact tympanic membrane. In addition, the presence of debris, masses or hyperplastic tissue in the external acoustic meatus may hamper visualization of the tympanic membrane. [27] The intact status of the tympanic membrane does not rule out the possibility of middle ear disease.

The most common imaging technique used is routine radiographic evaluation of the skull. Radiographic evaluation of the tympanic bullae and petrous temporal regions may provide information of value in the workup of middle ear disease. [52] General anesthesia is usually required to allow for proper positioning and to obtain quality radiographs. A high detail, good latitude film-screen system should be used to allow the visualization of subtle radiographic changes. [52] Routine radiographic views of the tympanic bulla include a dorsoventral (DV) or ventrodorsal (VD), laterolateral (lateral), a rostroventral-caudodorsal open mouthed oblique (R30° V-CdDO) and lateroventral-laterodorsal oblique (Lt20° V-RtDO and Rt20° V-LtDO). The dorsoventral view is accomplished by positioning the dog in sternal recumbency with the head on a cassette. The head should be positioned so that the mandibles are resting on the cassette, the center of the central axis is on the nuchal crest caudally and the nasal philtrum rostrally. The hard palate should be parallel to the film. In this view, the bulla may be partially masked due to superimposition of the petrous temporal bone. [53] This will cause the bulla to appear thicker and more radiopaque than in other views. The dorsoventral view is preferred to the VD view as the mandibles offer support that reduces rotation of the skull, and magnification of the area of interest is reduced. [53] The animal is placed in lateral recumbency to obtain the lateral and lateral oblique views. In lateral recumbency, the nose must be elevated to keep the skull parallel to the film. The hard palate and areas of

the orbit should be perpendicular to the film. The central axis of the x-ray beam should be placed on the horizontal ear canal and the field of view should include the calvarium, nasopharynx and larynx. [52] The lateral oblique views are obtained with the side of interest closest to the film. The ventral aspect of the skull is elevated to rotate the median plane approximately 20° from the lateral position. The position of the x-ray beam is the same as the lateral view. In order to perform the rostrocaudal open mouth oblique view, the animal should be placed in dorsal recumbency and the atlanto-occipital joint flexed so that the caudal aspect of the skull is parallel to the film. The mouth is then opened and the mandible is pulled caudally so that the central axis of the x-ray beam bisects the angle of the opened temporomandibular articulation. [52] The tongue and endotracheal tube should be secured to the mandible to eliminate any superimposition. The x-ray beam is centered on the median plane of the skull. The angle of the hard palate relative to the film may be altered to minimize overlying bony structures on the tympanic bulla. With brachycephalic breeds, the x-ray beam may need to be angled up to 20° dorsal to the hard palate in order to project the bulla tangentially.

In conventional radiography, normal bullae appear as thin-walled, symmetrical bone opacities with a relatively smooth external border. [52] The tympanic bulla lumen should be radiolucent along with the ear canal extending to the bullae on the DV view. If the animal has unilateral pathology, it may be helpful to compare the affected bulla to the unaffected side. [54] The rostrocaudal view allows good visualization although it is technically more difficult than the DV view. [53] There are multiple characteristic radiographic changes associated with middle ear disease but not all are present consistently. Increased soft tissue opacity within the bulla may occur with the accumulation of exudates or proliferation of soft tissues. [52] This will cause the lumen of the bulla to lose its air opacity. [53] The proliferation of soft tissues may be related to chronic inflammation, extension of hyperplastic tissue from the external ear, or neoplasia. Sclerosis and thickening of the tympanic bulla can also occur and is usually related to

chronic otitis media with the activation of osteoblasts. Various inflammatory mediators can activate osteoblasts; however, this change can also be seen with other disease processes such as nasopharyngeal polyps and craniomandibular osteopathy. [36] Lysis of the bulla or petrous temporal bone is suggestive of an aggressive process such as osteomyelitis from infection, or resorption due to neoplasia or a cholesteatoma. An occasional radiolucent fracture line with or without displacement will be seen secondary to the lysis. [52] If the middle ear disease is associated with external ear disease, then the external auditory canal may be calcified and show evidence of increased opacity within the external acoustic meatus. Additionally, a change in the shape of the tympanic bulla contour may suggest evidence of middle ear disease. Otitis media may increase the size of the bulla. [27] Advantages of radiography include its wide availability and lower cost when compared to computed tomography (CT). One of the main limitations of radiography is superimposition of other skull structures over the bulla. The complex anatomy of the tympanic bullae and the subtle nature of radiographic changes seen early in the disease process will commonly cause radiographic underestimation of the severity of disease in the middle ear. [52] One study compared radiographic versus surgical diagnosis of otitis media. In this study, it was found that radiography underestimated the number of dogs that had otitis media by 25%. [55] The author concluded that radiography could not be regarded as a highly sensitive tool in the diagnosis of otitis media. There were no false positive radiographic findings with this study. This suggests that radiography can be highly specific in the diagnosis of middle ear disease. In another study comparing radiography and computed tomography in the evaluation of otitis media in the dog, radiography again underestimated the number of tympanic bullae that were found to be abnormal on surgical examination. [56] Another limitation of skull radiography is that a surgical plane of anesthesia is required in order to achieve accurate positioning.

Computed tomography (CT) is an imaging technique that allows cross-sectional (transverse slice) viewing of the external, middle and internal parts of the ear. [53] This

removes confusing superimposed opacities to allow clearer visualization of the base of the skull and tympanic bullae. [52] Manipulation of the window and level settings of the digital image allows better visualization of tissues with different densities. Ideally, the skull position should be precise to allow comparison of symmetry unless a three dimensional slice orientation feature is available. [53] For transverse images, the anesthetized dog is placed in sternal recumbency with the head positioned on a radiolucent sponge in the center of the CT gantry. Radiolucent sponges, tape and other positioning devices can be employed to maintain the head position and keep the animal in sternal recumbency. To minimize artifacts caused by objects in the field of view of the x-ray beam, only the head should be in the gantry. The forelimbs should be pulled caudally.[52] Using a thin slice collimation and increment can optimize imaging of bony structures of the middle and inner ear. [53] The study is acquired by obtaining contiguous images of 1-3 mm slice thickness with an overlap of 1 mm beginning immediately rostral to the tympanic bulla and continuing to the level just caudal to the petrous temporal bones. [57] Because of the small size and detailed nature of the bullae, selection of the smallest field of view and a high mAs, high kVp technique should be used. [52] The use of a high kVp setting will help reduce beam hardening and streak artifact and a high mAs setting reduces visible noise. [53] The petrous temporal bone is one of the highest density bones of the body; therefore, strong beam filtration is used to minimize beam hardening and high-density streak artifacts. [53] Images are reconstructed with a high-resolution algorithm to maximize image resolution and to keep pixel size small. Edge enhancement can be used to increase the subjective sharpness of the bony structures. [53] Contrast-enhanced CT of the middle ear is not routinely performed, but if inner ear disease is suspected it may be warranted. [52] Post-contrast scans should be acquired with a standard resolution mode and thicker slices.[53] Contrast will routinely enhance neoplastic and inflammatory lesions and can help to differentiate them from necrotic debris and exudate accumulation. [53] High-resolution algorithms and thin slice settings result in a low signal-

noise ratio which may be suboptimal for viewing soft tissue structures of the ear that are typically evaluated after contrast enhancement. The standard algorithm and thicker slices will enhance the narrow range of contrast between fluid, normal soft tissue and abnormal contrast uptake of soft tissues. [53] Bone is typically evaluated with a wide window width and level [W=2000-3000, L=200-300 Hounsfield units (HU)]. Soft tissue structures are better visualized using a narrow window width and a level in the soft tissue range (W=400-800, L=100-300 HU). Reconstruction in orthogonal planes or three-dimensional views can also be performed. These additional views may be helpful for assessment of the extent of the lesion for radiation and surgery planning. [53] Reconstructed views will have poorer image resolution than the original scan plane. If warranted, an additional dorsal scan can be performed. This is accomplished by placing the dog in right lateral or dorsal recumbency, with flexion of the neck so that the hard palate is parallel to the scan plane. The head is held in this position with tape and radiolucent restraining devices. This will produce a detailed image of the skull in a coronal plane.

Computed tomographic characteristics of canine middle ear disease are similar to those described for conventional radiography. Evaluation for increased soft tissue or fluid within the bulla, the presence of osteolysis or osteoproduction and changes in the bulla contour should be performed. As with radiography, interpretation of CT images is done by comparing the affected side with the unaffected side or comparing images to a known normal. [53] A previous study comparing the wall of a fluid-filled bulla with that of an air-filled bulla showed that the fluid-filled bulla appeared consistently thicker. [58] The effect was more apparent when images were acquired as thick slices, reconstructed with a soft tissue algorithm, or displayed with a narrow window (< 250 HU). [58] Authors attributed the apparent increase in thickness to: 1) blurring effect associated with back projection reconstruction 2) increase in modulation transfer associated with lower spatial frequency objects and 3) partial volume averaging artifact. This artifact must be considered when interpreting fluid-filled bullae on CT. [58] The advantages of CT when compared to

conventional radiography include: elimination of superimposition artifact, improvement of anatomic detail by providing high contrast images with excellent definition of bone and soft tissue, and the use of heavy sedation instead of general anesthesia in some patients. Improved anatomic detail allows greater visualization of inner ear structures including the bony ossicles. Computed Tomography may be superior to magnetic resonance (MR) imaging when evaluating any changes of the inner and/or middle ear effecting bone structures. [53] The main limitations of CT versus radiography are its higher cost and selective availability. Few studies in the veterinary literature have looked at the diagnostic value of CT for evaluating middle ear disease in the dog. In one study that compared CT to surgical diagnosis of canine otitis media, it was found that CT had a sensitivity of 83% and a specificity of 89%. [56] This result suggested that CT was slightly more sensitive than radiography at detecting otitis media. However, it was also less specific than radiography. In another study, CT was valuable in diagnosing an intracranial lesion secondary to otitis media/interna. [31] Computed Tomography was considered the most accurate method of identifying fluid within the tympanic bulla in another experimental study comparing the results of CT, radiography and ultrasound. [59] It also has been suggested that CT is an excellent technique for demonstrating small abnormalities of the thin and complex bony structures of the human middle ear. [60] Therefore, it is considered the imaging modality of choice in the study of conductive hearing loss. [61] Some sources suggest anecdotally that CT is an excellent means of depicting bony destruction associated with tympanic bulla tumors.

Magnetic resonance imaging (MRI) uses magnetic and radiofrequency energy to generate slice images of structures. Magnetic resonance imaging for the middle ear should include dorsal (coronal) and transverse plane images using T1 and T2- weighted sequences. [53, 62] T2 weighted fast spin-echo images are useful for identifying fluid because of its high signal intensity. [53] Pre and post-gadolinium images are obtained with T1-weighted fast spin-echo sequence. This sequence is helpful in detecting the blood-

brain barrier, hypervascular lesions and other soft tissue abnormalities. Magnetic resonance imaging may help differentiate peripheral from central vestibular involvement because it clearly depicts the brainstem without the degrading artifacts common to CT in this region. [63] Magnetic resonance images of the inner ear are best obtained using volume acquisition sequences with less than 2 mm slice thickness. [53] The normal bulla should appear as a signal void on all imaging sequences because it contains air bounded by cortical bone. [64] Middle ear disease is often characterized by contrast enhancement along the inner margin of the tympanic bulla due to the presence of vascularized tissue. [53] Appropriate MRI protocols should allow visualization of various pathologic lesions of the membranous labyrinth. [53] The diagnostic sensitivity of MRI for canine middle ear disease has not been reported. One case report describes the MRI findings of a dog with otitis media and suspected otitis interna. [65] In this case, otitis media was evidenced by an increased signal at the level of the petrous temporal bone on post-contrast T1-weighted images, lack of fluid signal in the semicircular ducts and contents within the tympanic bulla that were isointense to the brain with a narrow hyperintense rim on T2-weighted images. [65] Another study on the MRI appearance of the feline middle ear concluded that, for 8 cats (5 with middle ear disease and 3 healthy cats); Magnetic resonance imaging was helpful prior to surgery. [62] The author also suggested that MRI was superior to radiography, in that radiography had failed to identify abnormalities in two of the five cats with middle ear disease. [62] The main strength of MRI is its excellent soft tissue contrast. In humans, MRI is useful in some complex conditions affecting the middle ear, such as cholesteatoma and the postoperative ear, when the precise relationship between the dura and intracranial contents has to be assessed. [60] Magnetic resonance imaging limitations include poor evaluation of osseous changes of the bulla, increased cost of the procedure relative to radiography, and limited accessibility. In the human literature, CT was better than MRI in predicting the presence of cholesteatoma and glomus tumors in the middle ear. [66] [67]

Future Directions

As CT and MRI become more available for veterinarians, further comparisons between canine and human middle ear disease may become more important. Magnetic resonance angiography (MRA) sequences obtained by time of flight technique or with a bolus administration of Gd-DTPA, have been diagnostic in humans in particular situations such as a vascular anomaly associated with the middle ear. [60] Magnetic resonance angiography could be used in dogs for the same purpose. Recent reports in the veterinary literature have advocated the use of ultrasound in the evaluation of canine middle ear disease. [59, 68] The bone wall of the tympanic bulla is thin enough in dogs to allow the ultrasound beam to penetrate and it is possible to identify the presence of gas or fluid within the lumen. [68] Furthermore, the procedure can be performed using standard diagnostic ultrasound equipment and appears to be well tolerated by un-sedated animals. [68] In initial studies, evaluating whether ultrasound could consistently differentiate the presence of fluid from gas in the tympanic bulla of canine cadavers, ultrasound was found to be more sensitive than CT and radiography for identifying the presence of fluid.[59] However, additional work will be required to determine the ability of ultrasound to identify fluid within the tympanic bulla of clinical cases of canine otitis media. [59] Additionally, CT technology continues to advance. Current CT scanners have decreased scan times, multiple detectors, and progressive reconstruction algorithms. It will be important to continue to assess the impact that these changes have on the diagnosis of middle ear disease.

There have been many recent papers published in the human literature looking at new etiologic agents and pathophysiologic mechanisms for the development of otitis media. Two of these papers have studied the pathogenesis of specific bacterial infections that lead to otitis media. [69] [70] Knowledge of the molecular events related to these infections may allow better prevention and treatments. The role of inflammatory

mediators in middle ear disease has also been studied. [30] Initial studies suggest that inflammatory mediators released in the middle ear cavity can play a role in the pathogenesis of otitis media and can cause functional as well as morphological changes to the inner ear. [30] Cytokines, growth factors, neurotransmitters and IgE immunity have all been reviewed. [36] [71] These inflammatory mediators are responsible for localized inflammatory reactions associated with otitis media by acting as chemotactic agents for leukocytes, producing vasodilatation, and increasing vascular permeability. [38] One study concluded that inflammation associated with otitis media with effusion was mediated, at least in part, by the primary cytokines TNF-alpha and IL-1 beta. [72] Effusion alone can result in changes to the middle ear. In a study evaluating sterile and infective middle ear effusions, both resulted in diffuse irreversible changes in the lamina propria of the pars tensa. [73] Further understanding of the roles of these processes may facilitate advancement toward the prevention of middle and inner ear disorders. [30] Currently, there is a lack of knowledge concerning the interaction between the middle and inner ear. [29] Research in this area may be beneficial in preventing complications of otitis media such as otitis interna and meningoencephalitis.

Since otitis media is a common extension of otitis externa in dogs, evaluation of the pathogenesis of external ear disease in dogs may be key in reducing the incidence of otitis media. In one study that looked at breed variation in the histopathologic features of chronic severe otitis externa in dogs, it was found that Cocker Spaniels were unique in that they predominately had ceruminous gland hyperplasia and ectasia. [74] Increased understanding of the pathophysiologic characteristics and the mechanism of proliferative ear disease may result in new therapies directed at modifying cerumin gland kinetics. [74] Further research at the cellular level may aid in reducing or preventing the incidence of otitis media in dogs.

CHAPTER 2

A COMPARISON OF RADIOGRAPHY VERSUS COMPUTED TOMOGRAPHY IN THE DIAGNOSIS OF MIDDLE EAR DISEASE IN THE DOG*

Introduction

The diagnosis of middle ear disease can be challenging because history, clinical signs and physical exam findings are similar to those of external ear disease. The absence of the tympanic membrane on otoscopic exam can be strongly suggestive of otitis media; however, otoscopic exam is often hindered by excessive proliferative tissue and debris within the external ear canal. [56] Conversely, an intact tympanic membrane does not eliminate the possibility of disease in the middle ear. [27] Therefore, additional imaging diagnostics are essential for both the diagnosis of middle ear disease and in the formulation of treatment regimens. [56] Two imaging modalities most commonly used by veterinarians for the evaluation of canine middle ear disease are conventional radiography and computed tomography (CT). Radiography of the tympanic bullae can be very helpful in the diagnosis of otitis media and aids in the formation of treatment options. [28, 55] Radiographic changes such as a thickened, irregular bulla and soft tissue opacities within the normally aerated bulla are commonly seen with chronic cases of otitis media. Radiographic changes may be slow to develop with acute cases and may not be apparent for several weeks after onset. [27, 28, 55] A previous study comparing conventional radiography to surgical diagnosis of otitis media found that radiography was not very sensitive in diagnosing otitis media. False negative radiographic findings were seen in 25% of the surgically confirmed cases of otitis media. [55] These results suggested that a negative radiographic evaluation of the middle ear might not be a reliable indicator of whether or not surgery was necessary. More recently, the use of CT has been proposed as an alternative or supplementation to conventional radiography. [52] Computed

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tomography has several advantages over conventional radiography, including elimination of superimposed overlying structures and superior soft tissue differentiation. [52, 56] The results of a previous study comparing radiography and CT suggested that CT might be more reliable than radiography in the diagnosis of canine middle ear disease. [56] However, CT had both false negative and false positive results. The false positive results were not seen on the radiographic study and may have been related to the inability of the radiologist to distinguish external ear disease from middle ear disease. In light of the false results for both imaging modalities, the authors suggested that the relative value of the two techniques was similar. Since that paper was published, improvements have been made in CT scanning technology, such as thinner slice settings and edge enhancement algorithms. These changes may allow better assessment of middle ear disease than previously described. The objectives of this prospective study were to compare findings from CT and conventional radiography with findings from surgery and histopathology, and to evaluate the inter-observer variability for interpretation of each imaging technique.

Materials and methods

Sample population

This prospective study was conducted at the Virginia-Maryland Regional College of Veterinary Medicine Teaching Hospital between March 2001 and March 2003. The Institutional Animal Care and Use Committee approved the research protocol and clients signed a standard client consent form for admission of dogs into the study. The control group consisted of three clinically-normal research dogs. These dogs had no history of ear abnormalities and no evidence of otitis externa on otoscopic exam. Two of these dogs were used as controls in the imaging correlation study and 1 of these dogs was used as a normal reference for image reviewers. The clinically-affected group consisted of 31 dogs with a history of chronic, severe otitis externa and no history of previous ear surgery. These dogs were recruited by means of a letter sent to in-house clinicians and referring veterinarians. Upon admission, dogs were examined by a board-certified veterinary surgeon to determine if they were good candidates for TECA. To be included in the study, dogs also had to have a lateral or ventral bulla osteotomy and a histopathologic sample submitted from at least one bulla within 2 weeks of imaging.

Radiograph and CT Techniques

The tympanic bullae of all control and clinically-affected dogs were examined using conventional skull radiography and computed tomography (CT). Imaging of control dogs was performed immediately after they were euthanized at the conclusion of other research studies. Imaging of clinically-affected dogs was performed with the dogs under routine general anesthesia. The first author performed all radiographic studies and supervised all CT studies to insure consistency. The radiographic examinations consisted of a dorsoventral (DV) or ventrodorsal (VD), laterolateral (lateral), a rostroventral-caudodorsal open mouthed oblique (R30° V-CdDO) and lateroventral-laterodorsal

oblique (Lt20° V-RtDO and Rt20° V-LtDO) (Figure 1-5) [52]. Radiographs were obtained using 8mAs, 50-70 kVp and a detail screen-film combination[†]. All CT examinations were performed using an on-site, 4th generation CT scanner[‡]. Contiguous 2mm transverse slices were obtained at 1 mm intervals from the temporomandibular joints to the caudal margin of the petrous temporal bones [56]. Technique settings were: 150 image size, 130 kVp setting, 105 mA, and a sharp algorithm. Images were exposed onto laser film using soft tissue window (L100-300 W300-800) and bone window (L250-500 W3200) settings (Figure 6). For each 14X17 inch film, 12 image frames were displayed.

Image data recorded

Three veterinary radiologists (2 board-certified and 1 resident-in-training) served as observers for the imaging studies. Each observer independently evaluated radiograph and CT images for each dog. Radiographic and CT film sets were placed in separate jackets, identified by a research number, and randomized. Observers interpreted each set of films without knowledge of surgical or histopathologic diagnosis. For each bulla, observers used a visual analog scale of 150 mm (Figure 7) to record certainty and severity of the following characteristics: 1) bony proliferation or thickening of the tympanic bulla, 2) lysis of the tympanic bulla, 3) increased opacity within the bulla, 4) abnormal contour of the bulla wall, and 5) overall assessment of middle ear disease. Observers were provided with instructions on use of the visual analog scale and a set of confirmed normal radiographs and CT images to use as a reference guide. The observers were also allowed to consult anatomic references. [1, 75]

[†] Kodak Lanex Fine Screen/ T-Mat G/RA film, Eastman Kodak Company, Rochester, NY 14650

[‡] Picker IQ/Xtra, Picker International, Cleveland, Ohio.

Surgical data recorded

For each dog, TECA and bulla osteotomies were performed using previously published techniques. [23] Board-certified veterinary surgeons or residents-in-training performed the surgeries on clinically-affected dogs. The first author performed post-mortem surgeries on each of the control dogs. Surgical decision-making for clinically-affected dogs was based primarily on history and physical exam findings. Imaging findings were not used as principal criteria influencing surgical decisions. Surgical findings for each dog were recorded by the first author, using an intra-operative questionnaire.

Histopathologic data recorded

Histopathologic samples of the external ear canal, tympanic bulla lining and a small fragment of the tympanic bulla wall were collected at surgery. Samples for aerobic culture and susceptibility were also obtained when the surgeon felt they were indicated. All samples were fixed in a 10% solution of neutral buffered formalin. In addition, bone from the bulla was demineralized by immersion in TBA-2 solution[§] for 2-3days. The first author trimmed all samples as necessary, and then placed in cassettes for processing and sectioning. Samples were processed routinely by embedment in paraffin and sectioned at 5 ∝m before staining with Hematoxylin and Eosin (H&E). A board-certified veterinary pathologist (RD) served as observer for all histopathologic samples. The pathologist re-evaluated samples in random order, without knowledge of group status or surgical findings. The same visual analog scale that was used by radiologists was used to rate histopathologic certainty and severity of middle ear disease. Microscopic assessment of the external ear tissues was also performed by the pathologist in clinically-affected dogs for inclusion in the medical record.

[§] Shandon Lipshaw, Pittsburgh, PA.

Data analysis

Diagnostic sensitivity of modalities

For each ear, middle ear disease certainty scores from each observer were calculated by measuring the distance from the zero mark to the observer's mark on the visual analog scale. Middle ear disease was considered to be absent in radiographic and CT images if at least 2 radiologists marked the associated visual analog scale at $\leq$ 60 mm. Middle ear disease was considered to be present if at least 2 radiologists marked the scale at $\geq$ 80 mm. If at least 2 radiologists chose marks between 60-80 mm, findings were considered equivocal and dogs were excluded from sensitivity analysis. These same cutoffs were used for the visual analog scale marks made by the pathologist. Surgical presence or absence of middle ear disease was determined by a consensus opinion from 2 evaluators (JR, DW), based on data recorded in the surgical questionnaires. Middle ear disease was determined to be present if the following findings were recorded: exudate in bulla, internal bulla bone proliferation or lysis, thickening of the tympanic bulla lining, or hyperplastic proliferative epithelium extending into bulla from the external ear canal. Data from operated ears were used to calculate sensitivity, specificity, and positive and negative predictive values for radiography and CT[**]. Calculations were made first using findings from histopathology as the gold standard, and then repeated using findings from surgery as the gold standard.

[**] Sensitivity = [# of true positives / (# of true positives + # of false negative)] X100
Specificity = [# of true negatives / (# of false positives + # of true negatives)] X100
Positive Predictive Value = [# of true positives / (# of true positives + # of false positives)] X100
Negative Predictive Value = [# of true negatives / (# of false negatives + # of true negatives)] X100

Comparison between imaging modality and histopathology scores

A paired t-test[††] was used to test the null hypothesis that the mean bias from each imaging modality did not differ from the histopathologic score. The test was performed for right and left ears separately. The mean radiographic and CT scores were compared to the histopathologic score and to each other. A value of $P< 0.05$ was used to define significance. Bias plots were created for the different scores (certainty or severity) and sides (right or left) for each modality compared to the histopathologic score.

Correlation analysis[‡‡] was used to test the hypothesis that individual characteristics of middle ear disease were significantly associated with histopathology results. The correlation coefficient (r) was calculated for each criterion assessed by the observers. Scatter plots of the mean modality scores for each side compared to the histopathologic scores were evaluated. A value of $P < 0.05$ was used to define significance.

Inter-rater variability

Random effects analysis of variance (ANOVA)[§§] was used to test the hypothesis that variance among observers and among dogs for certainty and severity of middle ear disease would be lower with CT than radiography. Error estimates and a ratio of observer variation to dog variation were compared between the two imaging modalities and histopathology.

[††]Paired T-test. The SAS System® version 8.2, SAS Institute Inc., Cary, NC 27513
[‡‡]Correlation analysis. The SAS System® version 8.2, SAS Institute Inc., Cary, NC 27513
[§§] ANOVA. The SAS System® version 8.2, SAS Institute Inc., Cary, NC 27513

Figure 1. Dorso-ventral skull radiograph demonstrating normal tympanic bullae.

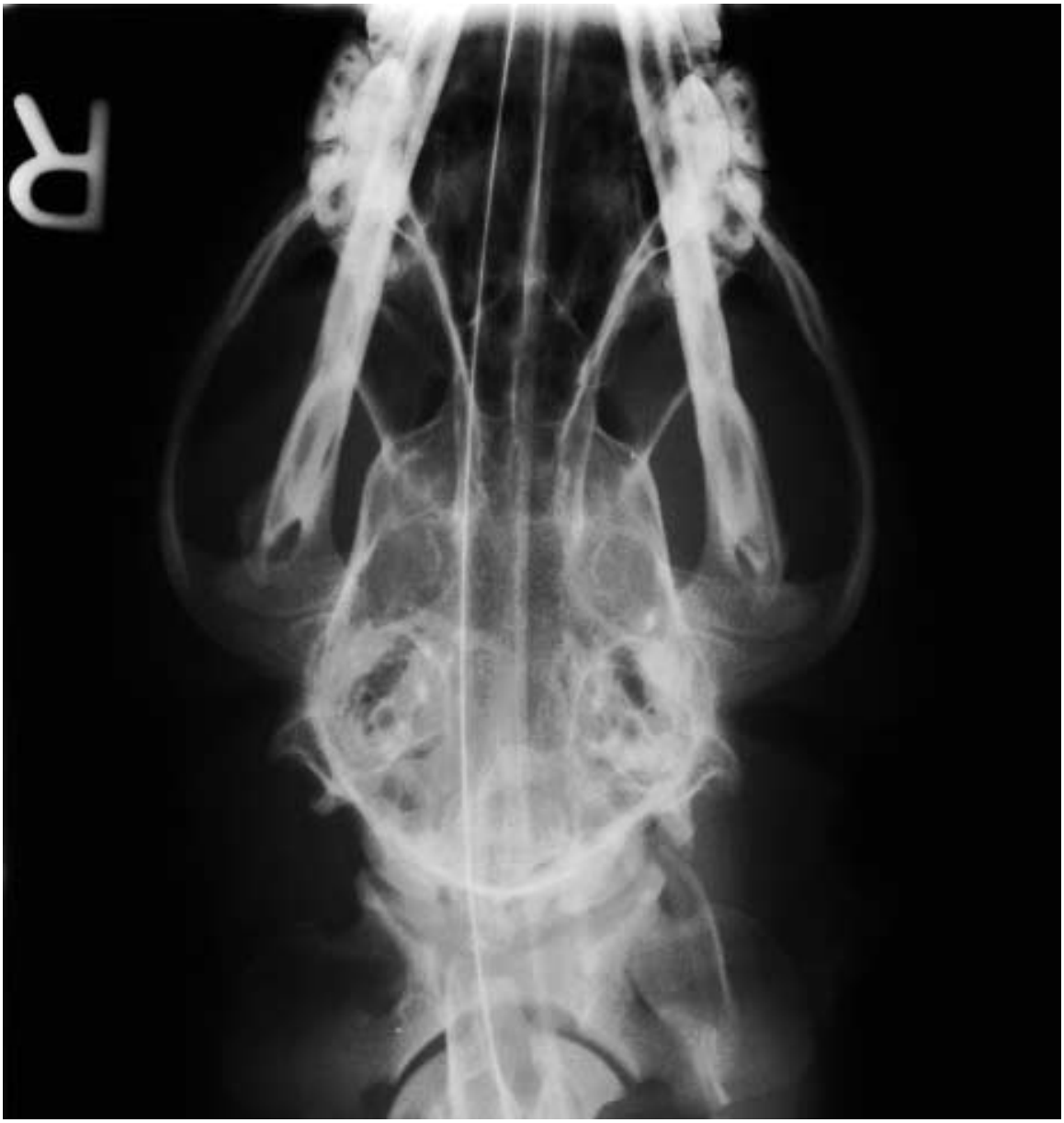


Figure 2. Laterolateral (lateral) radiograph demonstrating normal tympanic bullae.

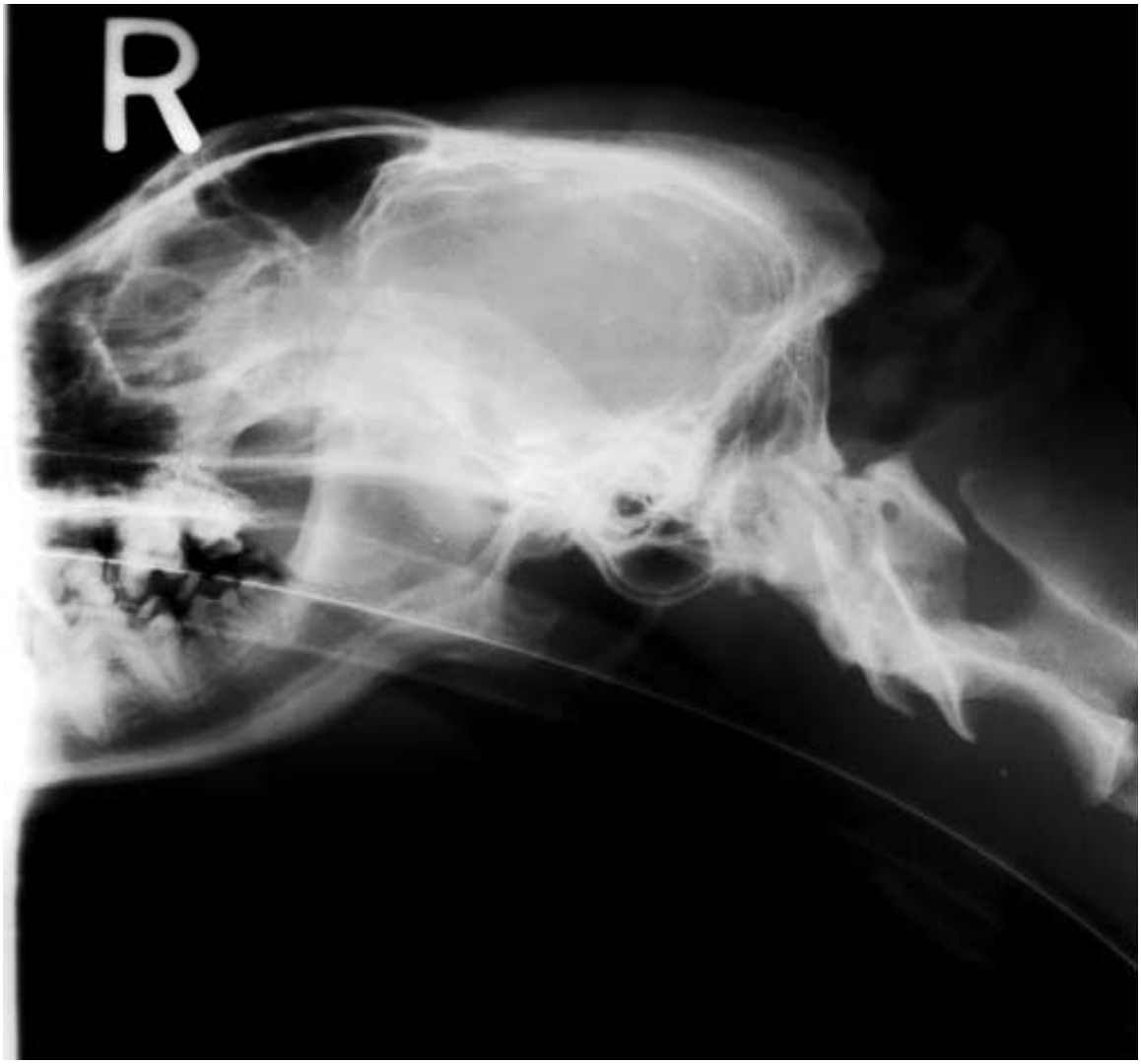


Figure 3. Left lateroventral-laterodorsal oblique (Lt20° V-RtDO) radiograph demonstrating a normal left tympanic bulla.

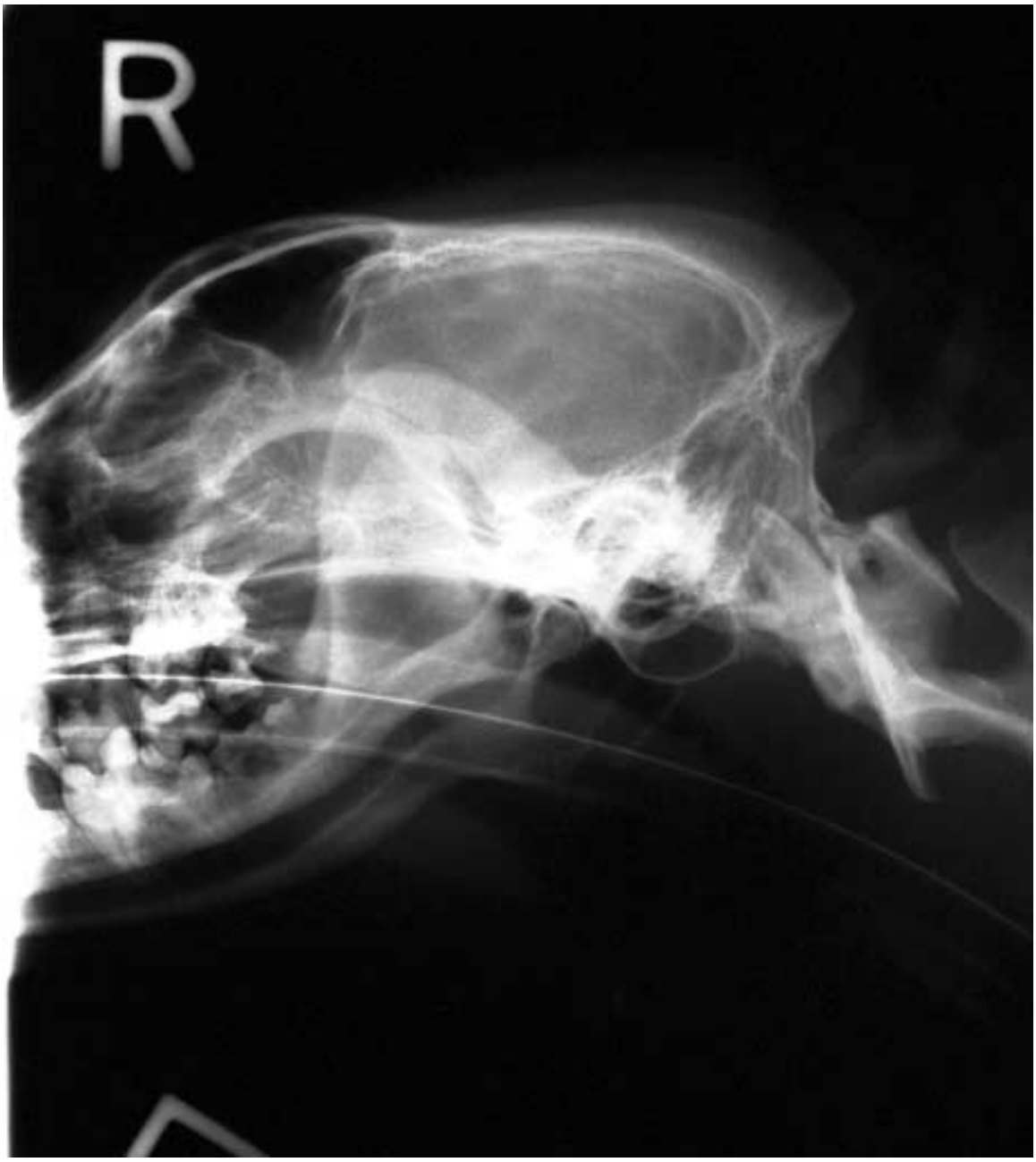


Figure 4. Right lateroventral-laterodorsal oblique (Rt20° V-LtDO) radiograph demonstrating a normal right tympanic bulla.

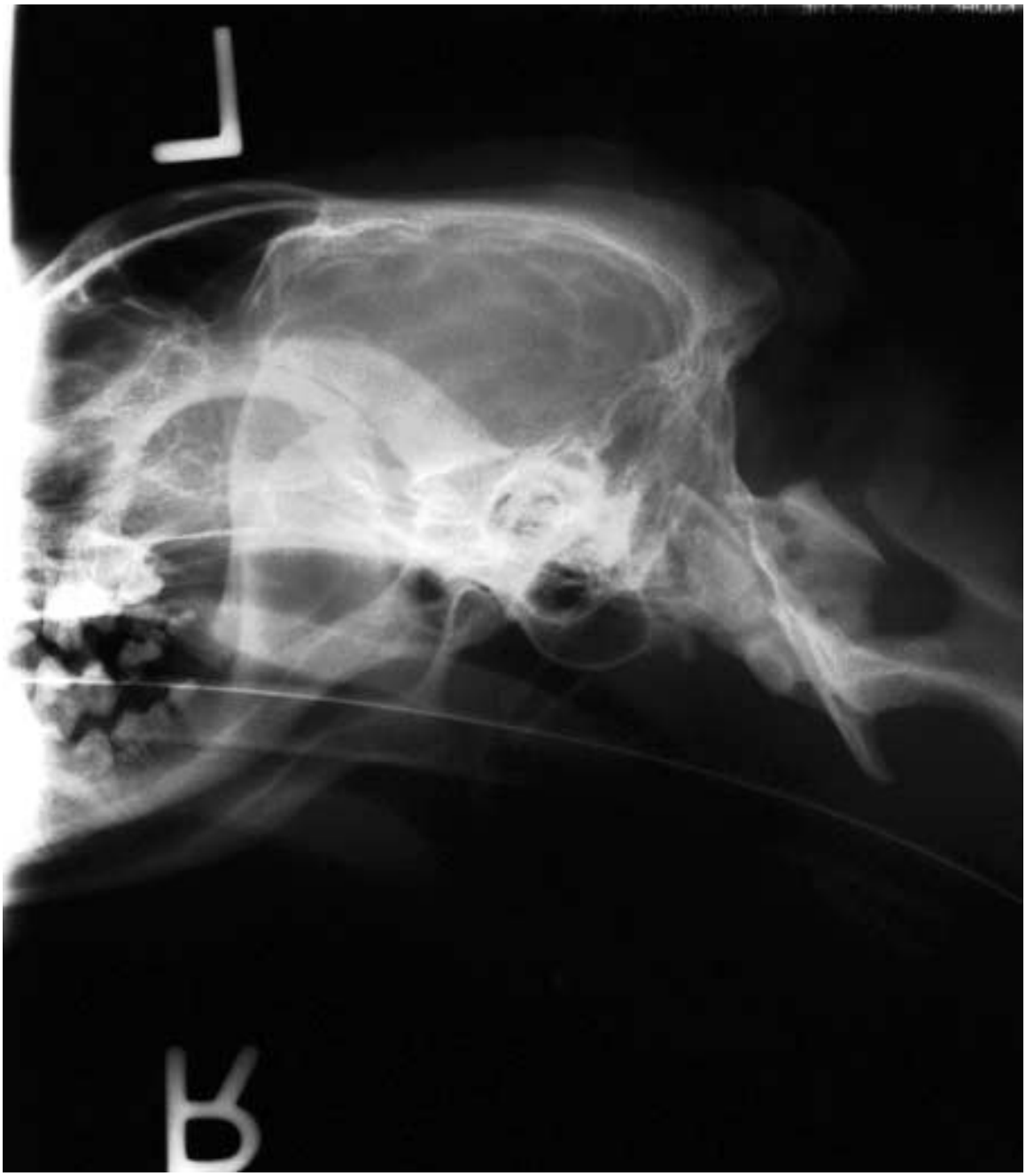


Figure 5. Rostroventral-caudodorsal open-mouthed oblique (R30˚ V-CdDO) radiograph demonstrating normal tympanic bullae.

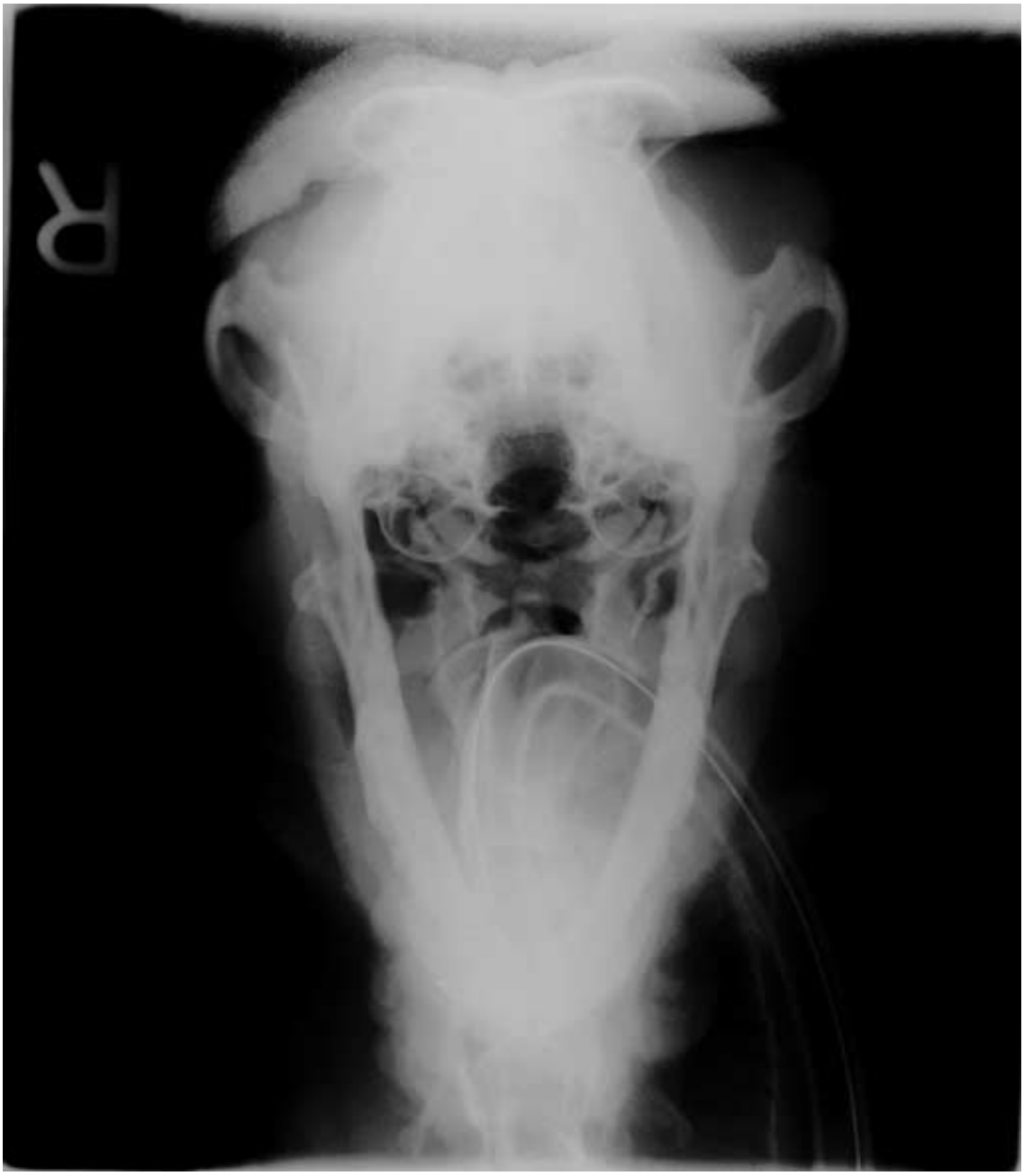
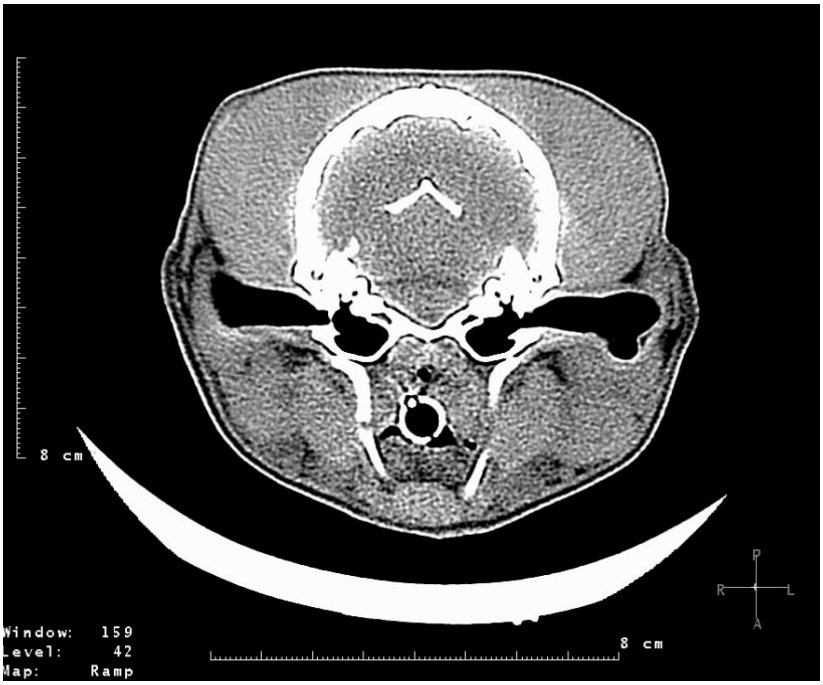


Figure 6. Transverse CT images from a normal dog filmed in a soft tissue and bone window.



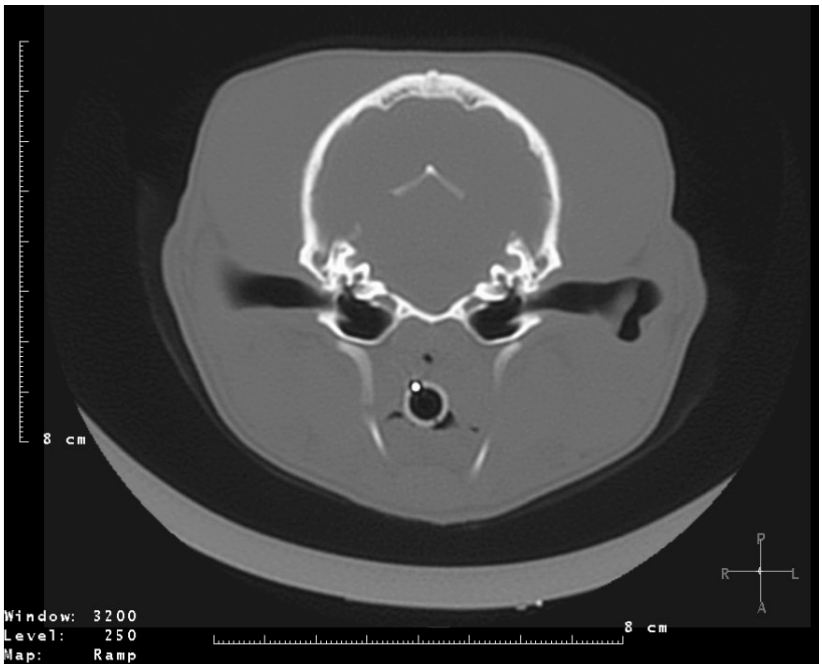
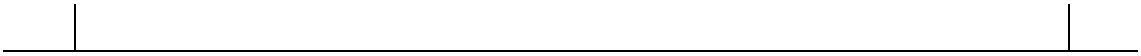


Figure 7. Visual analog scale used by radiologist and pathologist observers for a) certainty and b) severity of right middle ear disease. Observers could also record comments clarifying why they chose the score they did.

Middle ear disease, Right Side

a)

b)



Comments:

Results

Animals

There were 14 breeds represented in the clinically-affected group, with the most common being Cocker Spaniel (12 / 31, 39%), mixed breed (5 /31, 16%), Bassett Hound (2/31, 7%), and Labrador Retriever (2/31, 7%). Other breeds represented by one dog each were: Boykin Spaniel, Clumber Spaniel, Collie, English Cocker, English Setter, Miniature Poodle, Pomeranian, Saint Bernard, Shetland Sheepdog and Weimereiner. The gender distribution was 58% male and 42% female. Of the male dogs, 77% were neutered. Of the female dogs, 92% were spayed. The ages of the dogs ranged from 2 to 15 years with a mean age of 7.6 years. Surgery was performed on both ears for 15 of the 31 clinically affected dogs (48%). The other dogs had unilateral surgery, with 9 on the left side and 7 on the right. All dogs had lateral bulla osteotomy and TECA. The 3 control dogs were of mixed breed, with 1 male and 2 female. All control dogs were skeletally mature, but their exact age was not known. The three control dogs had bilateral surgery performed following euthanasia. One of these dogs was used as the normal reference for the observers of the imaging modalities. Data from the remaining two control dogs were used in statistical analyses.

Radiograph and CT Evaluation

In 29 cases, the radiographs and CT scans were performed on the same day as the surgery. In 4 cases, surgery was performed within 11 days of the diagnostic imaging studies. In 2 cases, the diagnostic imaging studies and surgery on one ear were done on the same day but the opposite ear was operated on a different day. One of these cases had surgery on the contralateral ear 2 days later and the second case had surgery 47 days later. Both of the latter had anesthetic complications during surgery that prevented

prolonged anesthesia time. Both bone and soft tissue window images were available for all but one dog. This dog was only filmed using a bone window setting. Attempts to retrieve the case and print the study in a soft tissue window failed due to corruption of the storage device.

Surgical and Histopathologic Evaluation

A total of 50 bullae were examined surgically. In the clinically-affected group, quality of surgical exposure of the tympanic bulla was recorded in 29 dogs and 44 ears. Quality of surgical exposure for 2 of the clinically-affected ears was not available due to either misplacement of the surgical questionnaire or absence of recorded information on the questionnaire. In the control group, quality of surgical exposure was not recorded. The exposure of the middle ear was considered to be poor in 2/44 ears (5%), adequate in 16/44 ears (36%), good in 9/44 ears (20%), and excellent in 17/44 ears (39%). Tympanic membrane integrity was recorded for 28/45 (62%) ears in the clinically-affected group. Of these, only one was found to be intact. Of the 50 bullae examined, 38 (76%) of the bullae were also evaluated by aerobic culture and susceptibility testing. Of these bullae, 16/38 (42%) had a positive culture. Culture results were as follows: mixed bacteria population (6/38, 16%), *Pseudomonas aeroginosa* (5/38, 13%), *Staphlococcus intermedius* (3/38, 8%), *Proteus mirabilis* (2/38, 5 %), and no growth (22/38, 58%). A total of 47 ears were included in the surgical sensitivity and correlation portions of the analysis (43 from the clinically-affected group and 4 from the control group). One clinically-affected ear was excluded from analysis due to misplacement of the surgical questionnaire. Two ears from the clinically-affected group were excluded from analysis due to equivocal surgical findings. A surgical diagnosis of middle ear disease was given for 29/47 ears (62%). Middle ear disease was considered to be absent in 18/47 ears (38%). Post-surgical complications recorded in the medical records of the clinically-

affected dogs included incomplete or decreased palpebral reflex, facial nerve paralysis or paresis and swelling at the surgical site.

Histopathologic samples were collected from a total of 50 ears (46 from clinically-affected dogs and 4 from control dogs). Eighteen of the these ears (36%) were excluded from the histopathologic portion of the analysis, either due to insufficient middle ear tissue or indeterminate origin of the tissue sample (middle ear versus external ear). Of the remaining 32 ears, 28 (88%) were considered positive for middle ear disease and 4 (12%) were considered negative. Varying degrees of inflammatory disease (otitis media) were seen in 25/28 of the positive samples (89%) and neoplastic disease was seen in 3/28 of the positive samples (11%). Neoplasms identified were: mixed ceruminous adenoma, ceruminous adenocarcinoma, and basosquamous carcinoma. One bulla wall sample had evidence of osteomyelitis. Three of the 4 normal samples were collected from the control dogs. One sample from a control dog exhibited evidence of mild otitis media. For 7 bullae, surgical and histopathologic diagnoses differed. All of these samples had evidence of mild inflammation of the tympanic bulla lining on histopathology.

Statistical Analysis

Diagnostic sensitivity of modalities

A total of 32 bullae (28 abnormal and 4 normal) were included in the sensitivity analysis using histopathology as the gold standard. When histopathology was used as the gold standard, radiography correctly identified 15 of 28 abnormal bullae and 4 of 4 normal bullae. There were no radiographic false positives but there were 13 false negatives. Computed tomography identified 18 of 28 abnormal bullae and 4 of 4 normal bullae. There were no false positives and 10 false negatives. A total of 47 ears (29 abnormal and 18 normal) were included in the sensitivity analysis using surgery as the gold standard. Radiography correctly identified 16 of 29 abnormal bullae and 13 of 18

normal bullae. There were 3 false positives and 15 false negatives. Computed tomography correctly identified 25 of 29 abnormal bullae and 16 of 18 normal bullae. There were 2 false positives and 4 false negatives. Sensitivity, specificity, and positive and negative predictive values are tabulated in Table 1.

Comparison between imaging modality and histopathology scores

When certainty of middle ear disease for the left side was compared between radiography and histopathology, a bias plot demonstrated an upward trend with the radiology score increasing as the histopathology score increased (Figure 8). The paired T-test analysis for this side showed that the radiograph and the histopathology scores did not differ (P=0.1138), this indicated that the certainty scores for radiography and histopathology agreed for the left side. This was also true when certainty scores for CT and histopathology were compared for the left side (P value = 0.0756). The bias plot for CT and histopathology also showed a general upward trend (Figure 9). For certainty of right middle ear disease, the P values for radiology and CT versus histopathology were <0.0001 and 0.0011 respectively. This indicated that the radiographic and CT scores were significantly different from the histopathology scores for the right side. Bias plots of both modalities showed a general upward trend and underestimation of the certainty scores for both CT and radiography when compared to histopathology (Figures 10 and 11). Results of the middle ear disease severity comparison in the left side yielded P values for radiography and CT of 0.403 and 0.724 respectively. Again the bias plots for severity on the left side had a general upward trend (Figure 12 and 13). Both modalities were not significantly different from the histopathology for severity of middle ear disease on the left side. For severity of disease on the right side, the P values for radiography and CT were 0.0012 and 0.11 respectively. This indicates that the radiographic scores were significantly different from the histopathology scores but the CT scores were not. Comparison of bias plots for severity of disease for the right side (Figures 14 and 15)

versus the left side (Figure 12 and 13) yielded some differences. Although the bias plots for the right side still demonstrated a general upward trend, the severity scores for the right side tended to be less than the left. The scores for both imaging modalities also tended to underestimate the scores from histopathology. When compared to each other, radiograph scores did not differ significantly from CT scores. The P values for certainty were 0.458 for the right side and 0.621 for the left. Severity scores also did not show a significant difference. The P values for severity were 0.752 for the right side and 0.288 for the left side.

Correlation coefficients were calculated for all the individual radiographic and CT middle ear disease characteristics and compared to histopathology. Results are tabulated in Table 2. A positive correlation ($P < 0.05$) between the radiographic and histopathology scores was found for the following criteria of middle ear disease: 1) increased opacity certainty on the left side, 2) bulla proliferation severity on the right side, 3) increased opacity severity on the right side, and 4) change in bulla contour severity for the right side. A positive correlation was found between CT and histopathology scores for the following criteria: 1) increased opacity certainty for the left side, 2) increased opacity severity for the right and left sides, 3) bulla bone proliferation severity for the right and left sides and 4) change in bulla contour severity for the left side. Although these criteria had a positive correlation with histopathology, only a few of the scatter plots had a general upward trend that was suggestive of a positive correlation (Figure 16-17). When some of the other scatter diagrams were evaluated, an upward trend was suggested but there were outliers near the top right hand and left hand corner that may have skewed the result (Figure 18-21). In other scatter plots there is a random distribution of points with no clear indication of a positive linear relation between the variables (Figure 22-23).

Inter-observer variability

Variability among observers for each modality was assessed using a random effects ANOVA. The error estimates and ratio of observer variance to dog variance are summarized for both modalities in Table 3. The results demonstrated that there was some variation between observers for all of the criteria assessed with radiography while assessment with CT only had variation for some of the criteria. There was no detectable variability between rater scores for the following criteria when evaluated with CT: 1) middle ear disease certainty and severity for the left side, 2) certainty and severity of bulla bone lysis, and 3) severity of increased opacity within the bulla for the left side. Overall, variation of the scores between observers for middle ear disease was low when compared to the amount of score variation seen between dogs. Variability between observers accounted for less than 10% of the total variation in the assessment of middle ear disease certainty by both modalities. Overall score variation in assessing middle ear disease severity was less than 2% of the total variation when evaluated with CT and less than 21% of the total variation when evaluated with radiography. Individual criteria of middle ear disease had a broader range of variability. Variability between observer scores with radiography ranged from 1% to 60% of the total variation while variability with CT ranged from 0% to 16%.

Table 1. Diagnostic sensitivity and specificity of radiography and computed tomography for detecting middle ear disease.[***]

		Modality	
Test	**Gold Standard**	CT (%)	Radiography (%)
Sensitivity			
	Histopathology	64	54
	Surgery	86	55
Specificity			
	Histopathology	100	100
	Surgery	89	83
Positive Predictive Value			
	Histopathology	100	100
	Surgery	93	84
Negative Predictive Value			
	Histopathology	29	24
	Surgery	80	54

[***] For calculations using histopathology as the gold standard, N= 32 bullae. For calculations using surgery findings as the gold standard, N= 47 bullae. Formulas used for all calculations were as follows:

Sensitivity = [# of true positives / (# of true positives + # of false negative)] X100

Specificity = [# of true negatives / (# of false positives + # of true negatives)] X100

Positive Predictive Value = [# of true positives / (# of true positives + # of false positives)] X100

Negative Predictive Value = [# of true negatives / (# of false negatives + # of true negatives)] X100

Table 2. Correlation between visual analog scores for imaging characteristics versus scores for histopathologic certainty and severity of middle ear disease. Correlation coefficients |r| are presented for each criteria based on side and modality.

		Histopathology Certainty		**Histopathology Severity**	
Characteristic of Middle Ear Disease	Side	Radiology	CT	Radiology	CT
Bulla bone proliferation	R	0.233	0.099	0.561*	0.529*
	L	0.307	0.310	0.029	0.414*
Bulla bone lysis	R	0.143	0.018	0.431	0.336
	L	0.348	0.189	0.251	0.252
Increased opacity within the bulla	R	0.282	0.176	0.738*	0.553*
	L	0.406*	0.469*	0.189	0.521*
Change in the bulla contour	R	0.053	-0.002	0.533*	0.384
	L	0.251	0.331	0.236	0.451*

* Indicates significant value ($P < 0.05$)

Table 3. Comparison of inter- observer variability between radiography and CT for 33 dogs (50 ears). ANOVA was used to estimate the error between observers (Observer) and the ratio of observer variation to dog variation (ratio) when different characteristics of middle ear disease were evaluated. Variability between observers and the ratio to dog variation was also estimated for middle ear disease itself. Estimates and ratios are presented for each criterion based on ear side and imaging modality. †††

		Radiology		**CT**	
Characteristic of Middle Ear Disease	Side	Observer	Ratio	Observer	Ratio
Middle ear disease certainty	R	**126.14**	0.057	217.04	0.093
	L	71.32	0.025	**0**	0
Middle ear disease severity	R	184.11	0.202	**17.62**	0.013
	L	200.80	0.131	**0**	0
Certainty of bulla bone proliferation	R	**28.98**	0.012	634.73	0.305
	L	**56.54**	0.020	416.24	0.160
Severity of bulla bone proliferation	R	**101.18**	0.123	130.34	0.122
	L	**49.49**	0.042	144.67	0.132
Certainty of bulla bone lysis	R	62.62	0.099	**0**	0
	L	93.62	0.100	**0**	0
Severity of bulla bone lysis	R	57.32	0.203	**0**	0
	L	68.66	0.115	**0**	0
Certainty of increased opacity within the bulla	R	**104.72**	0.049	226.16	0.095
	L	**44.95**	0.016	163.97	0.056
Severity of increased opacity within the bulla	R	123.24	0.141	**5.81**	0.003
	L	139.28	0.108	**0**	0
Certainty of change in the bulla contour	R	540.60	0.483	**97.29**	0.053
	L	734.28	0.529	**111.43**	0.053
Severity of change in the bulla contour	R	240.60	0.599	**70.89**	0.081
	L	366.07	0.399	**77.33**	0.073

††† Numbers in **bold** had the lower variability of the two modalities.

Figure 8. Scatter bias plot comparing the certainty of middle ear disease on the left side between radiography and histopathology.

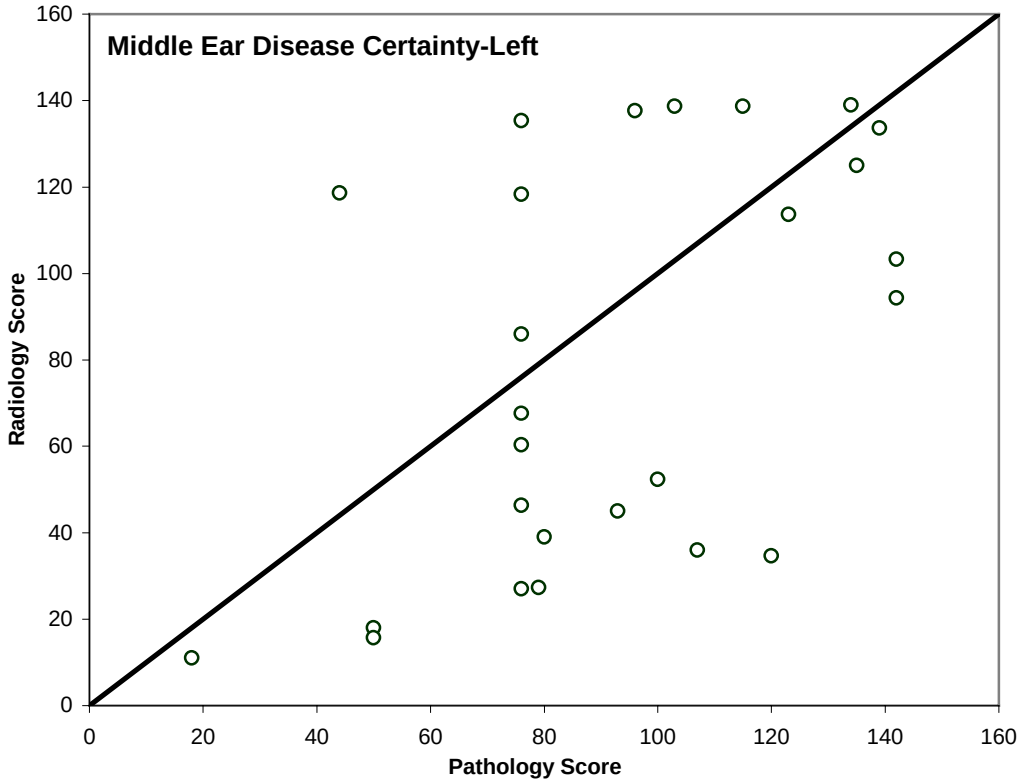


Figure 9. Scatter bias plot comparing the certainty of middle ear disease on the left side between CT and histopathology.

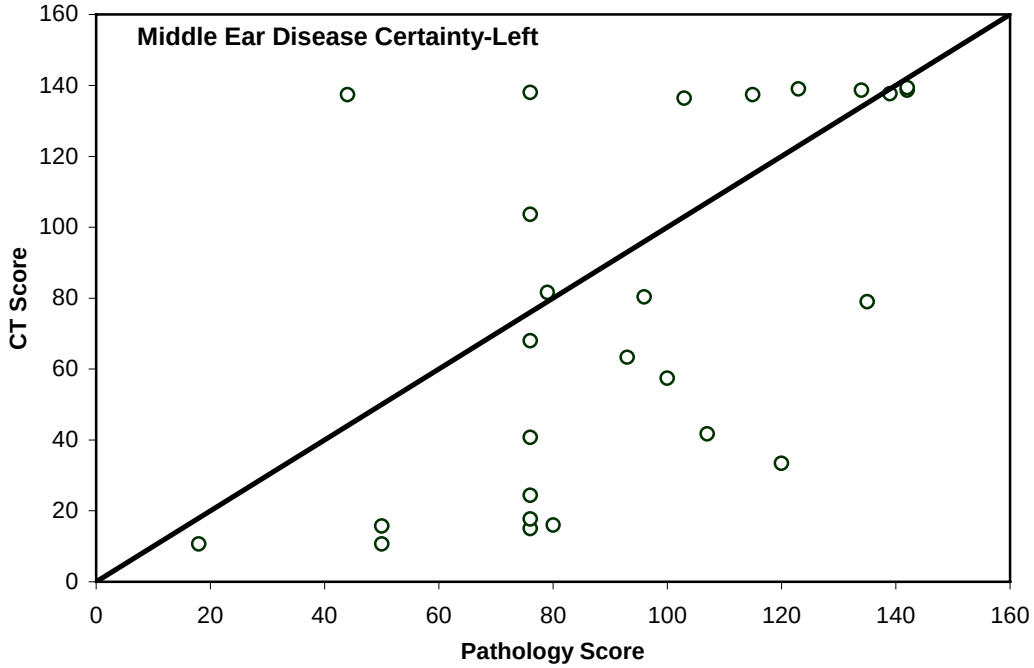


Figure 10. Scatter bias plot comparing the certainty of middle ear disease on the right side between radiography and histopathology.

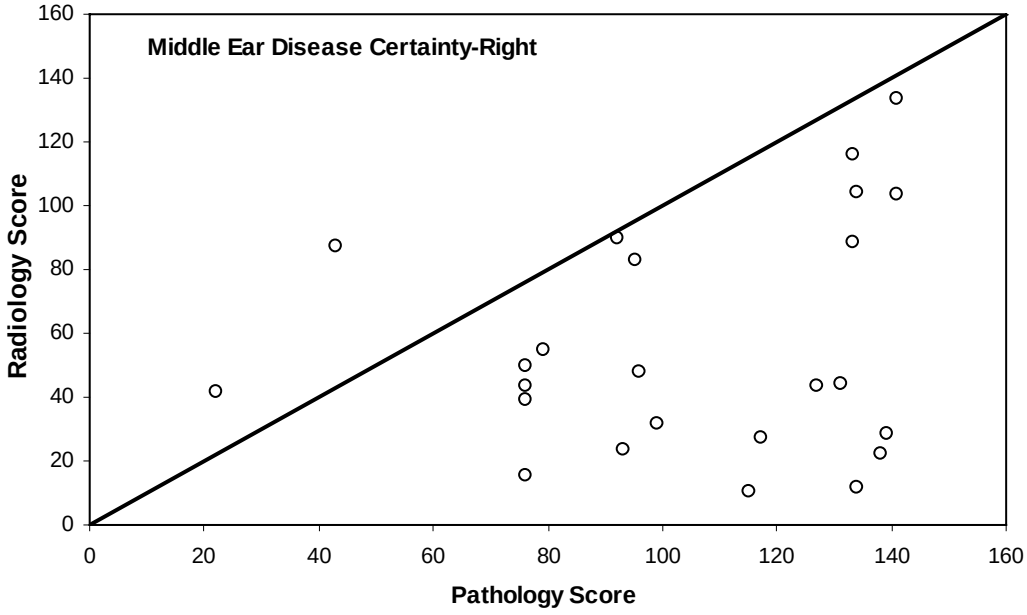


Figure 11. Scatter bias plot comparing the certainty of middle ear disease on the right side between CT and histopathology.

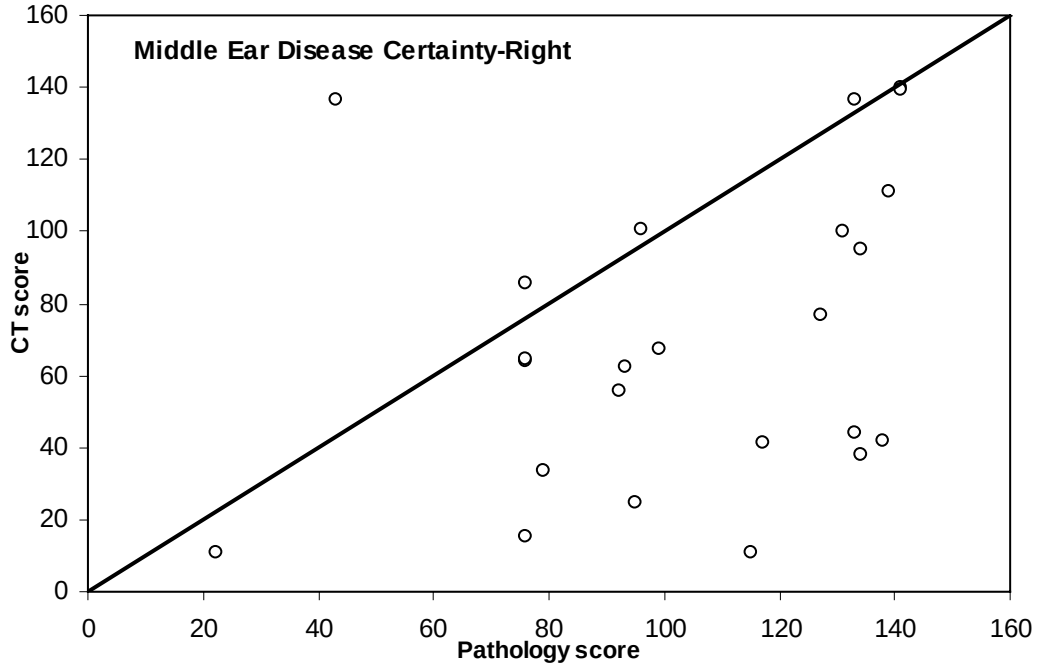


Figure 12. Scatter bias plot comparing the severity of middle ear disease on the left side between radiography and histopathology.

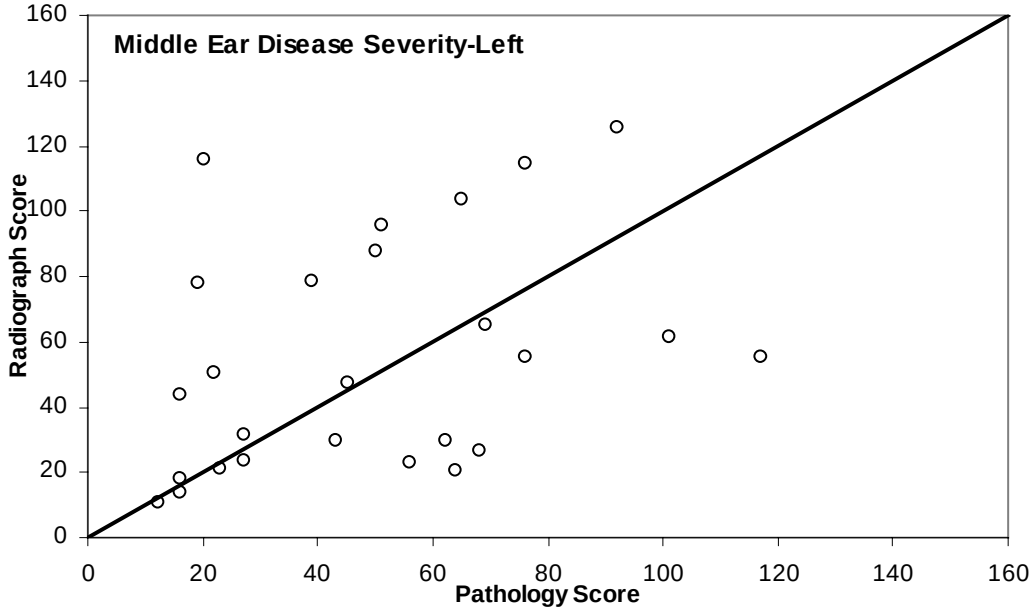


Figure 13. Scatter bias plot comparing the severity of middle ear disease on the left side between CT and histopathology.

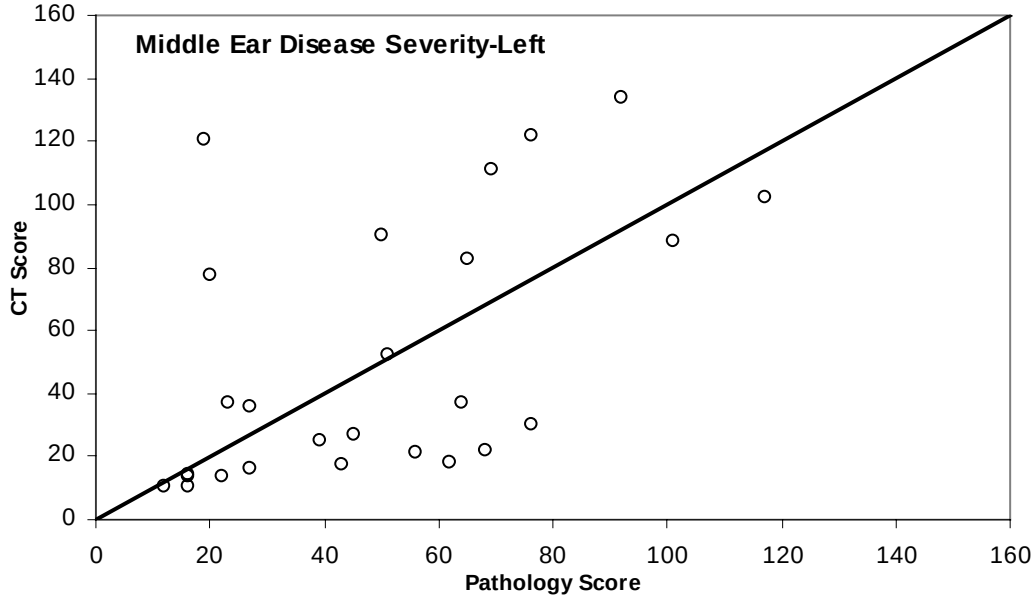


Figure 14. Scatter bias plot comparing the severity of middle ear disease on the right side between radiography and histopathology.

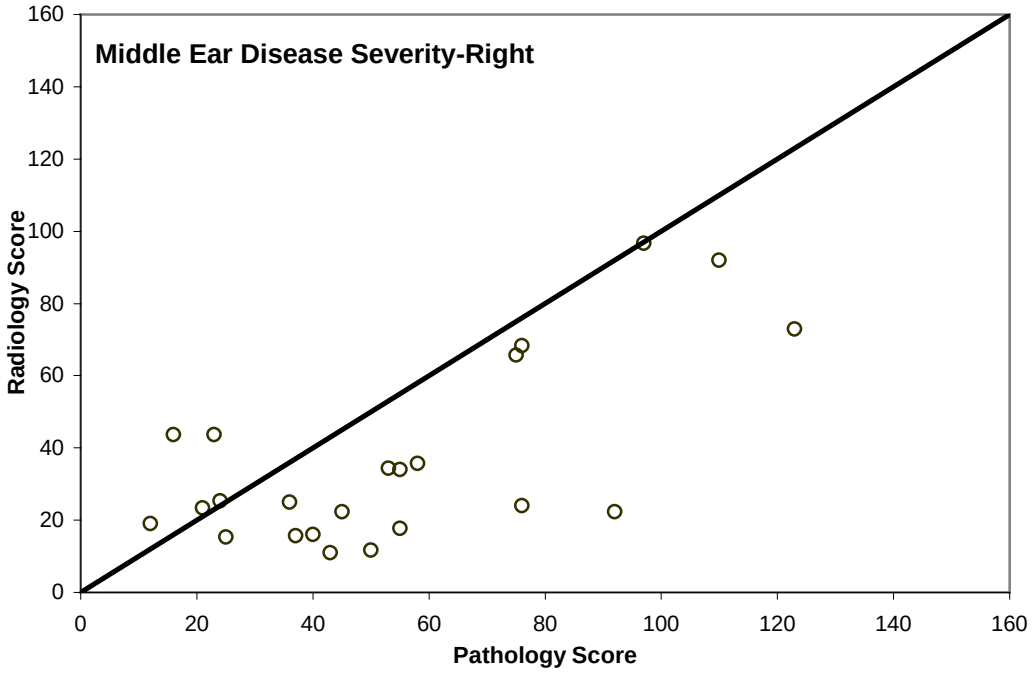


Figure 15. Scatter bias plot comparing the severity of middle ear disease on the right side between CT and histopathology.

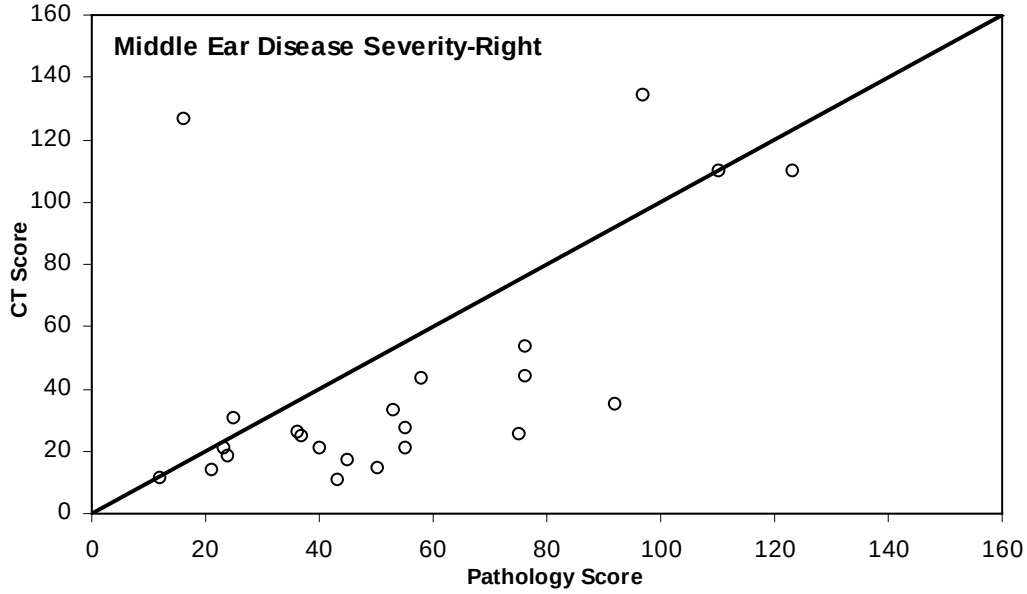


Figure 16. Scatter plot of radiographic increased opacity severity (R_IOS) compared to histopathology middle ear severity (Path_MEDS) for the right side.

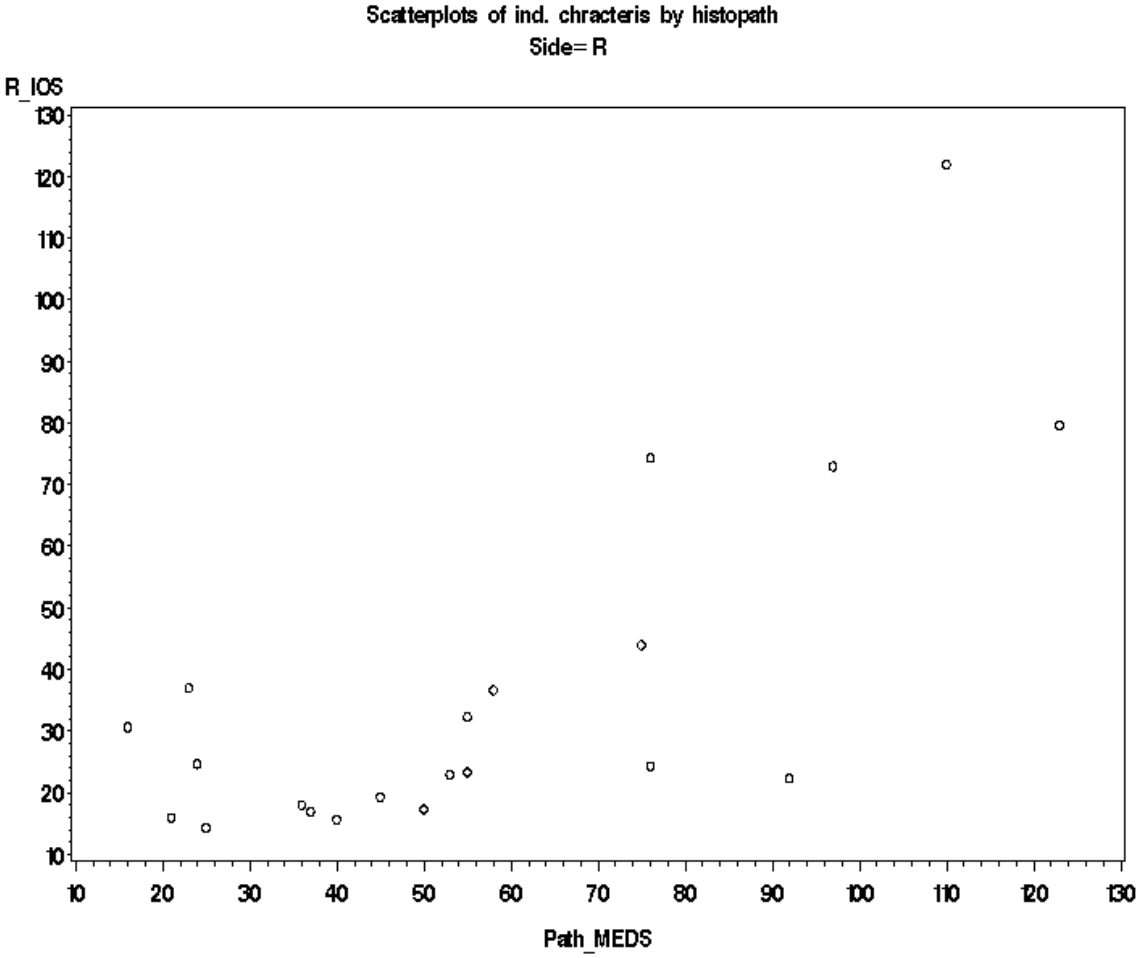


Figure 17. Scatter plot of radiograph bulla proliferation severity (R_BPS) compared to histopathology middle ear severity (Path_MEDS) for the right side.

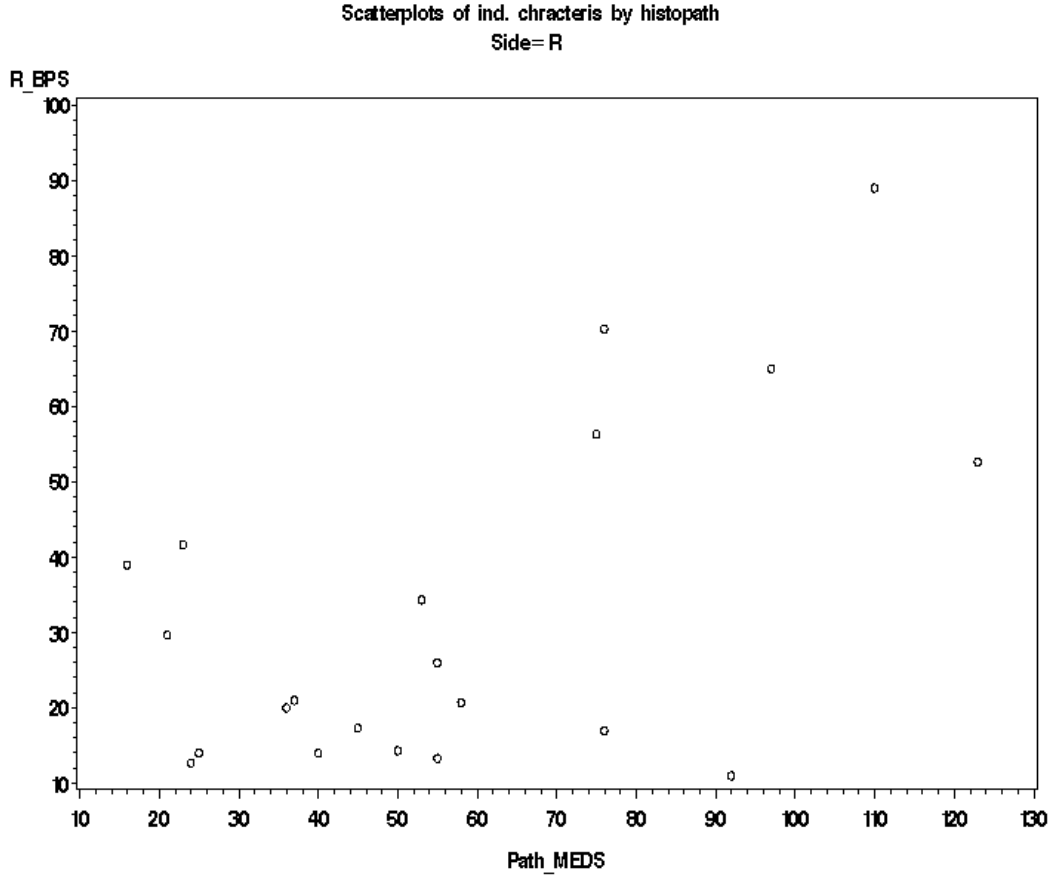


Figure 18. Scatter plot of CT increased opacity severity (CT_IOS) compared to histopathology middle ear severity (Path_MEDS) for the left side.

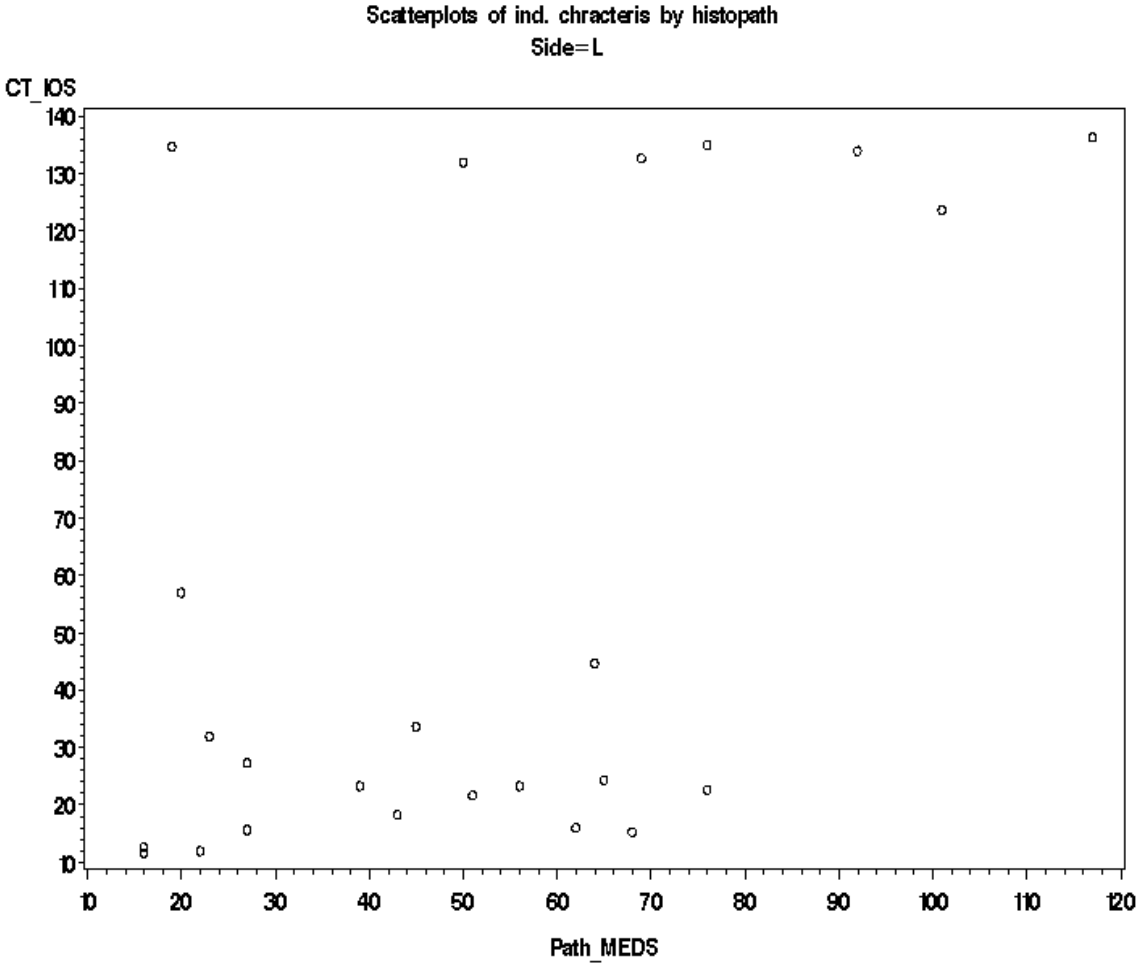


Figure 19. Scatter plot of CT increased opacity severity (CT_IOS) compared to histopathology middle ear severity (Path_MEDS) for the right side.

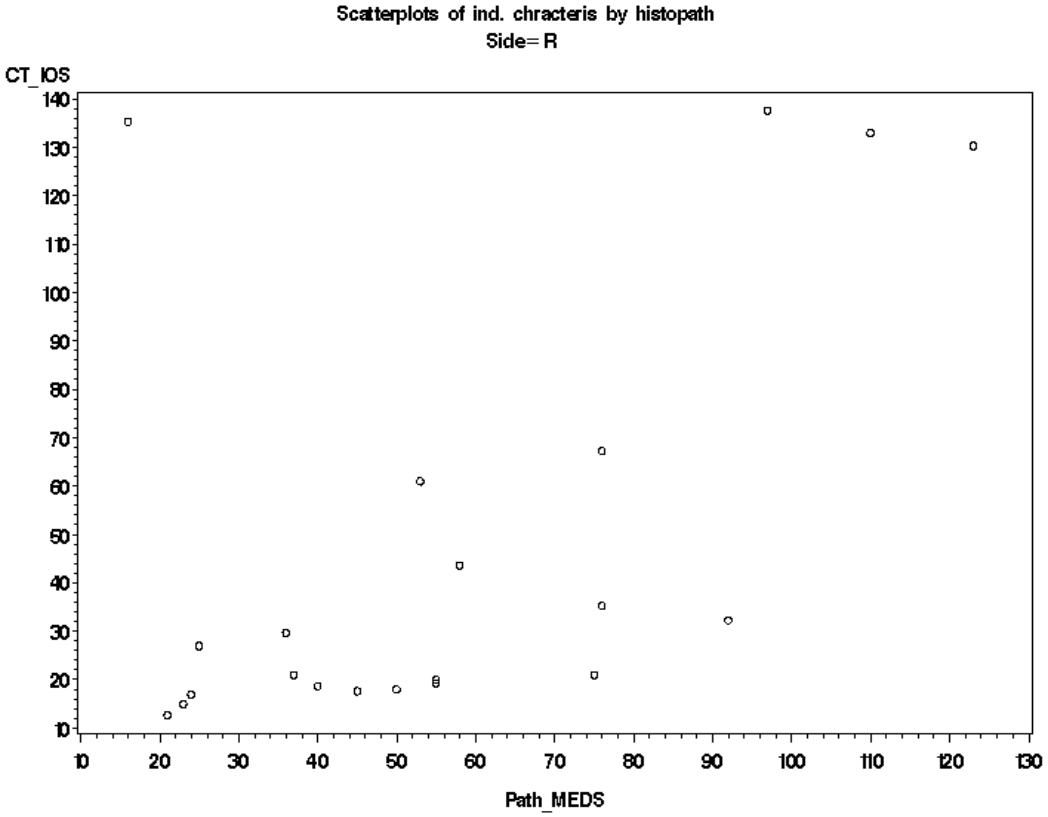


Figure 20. Scatter plot of CT bulla proliferation severity (CT_BPS) compared to histopathology middle ear severity (Path_MEDS) for the left side.

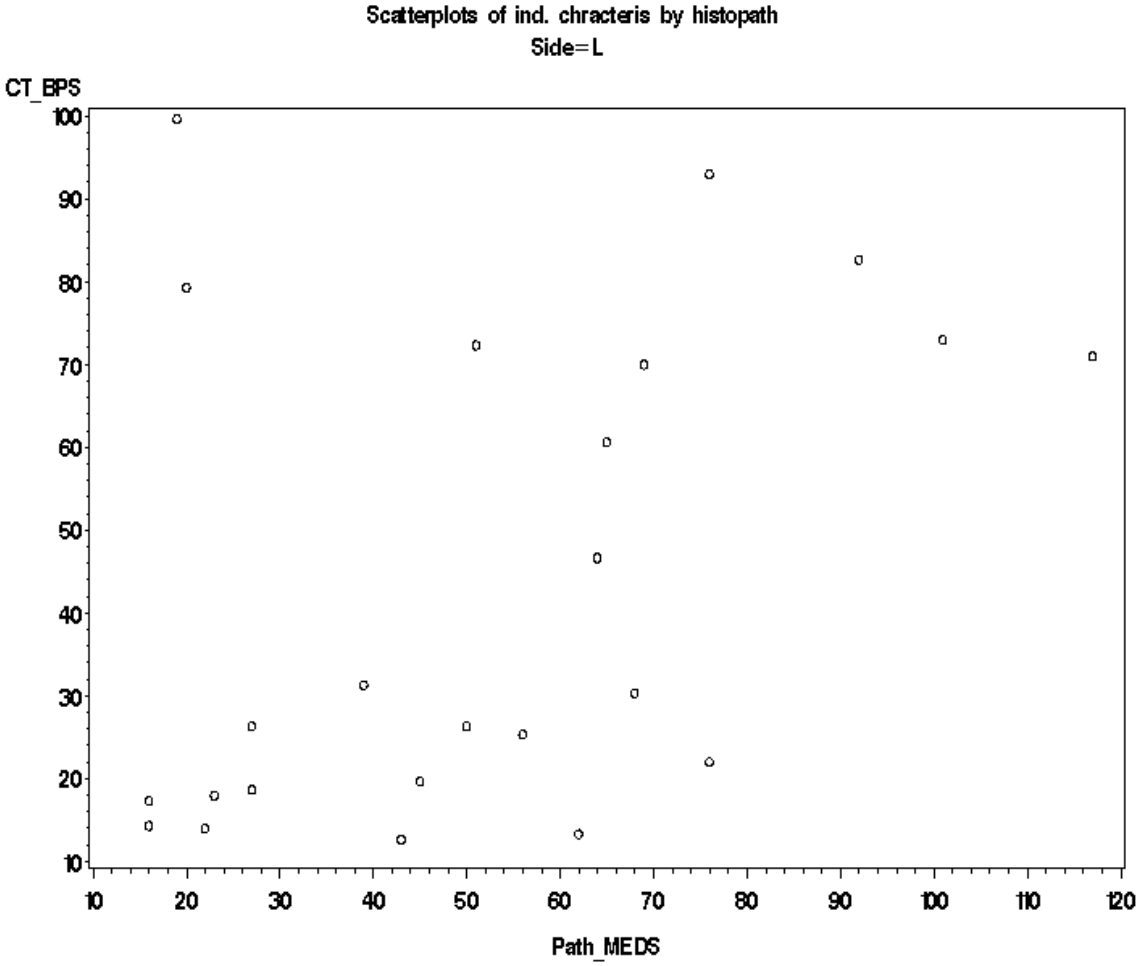


Figure 21. Scatter plot of CT bulla proliferation severity (CT_BPS) compared to histopathology middle ear severity (Path_MEDS) for the right side.

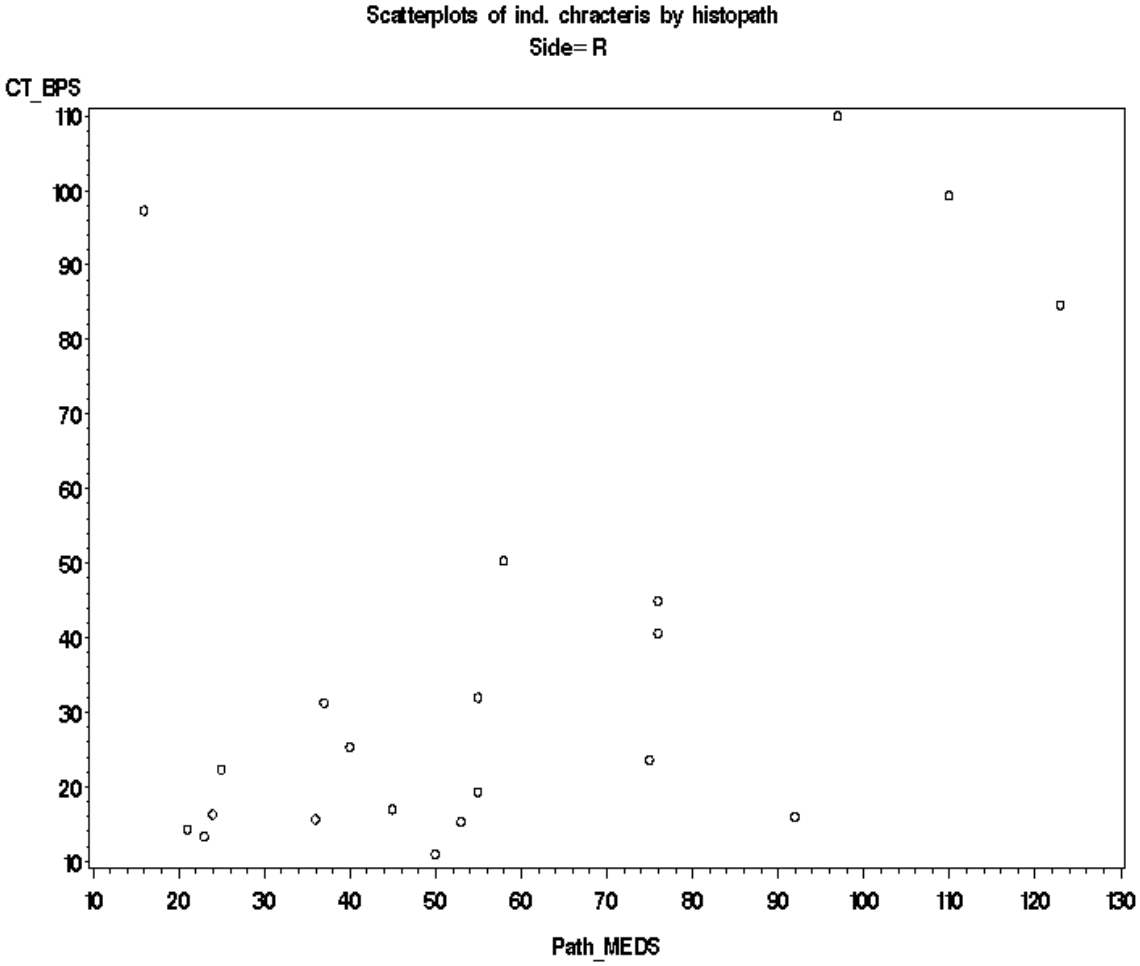


Figure 22. Scatter plot of radiograph increased opacity certainty (R_IOC) compared to histopathology middle ear certainty (Path_MEDC) for the left side.

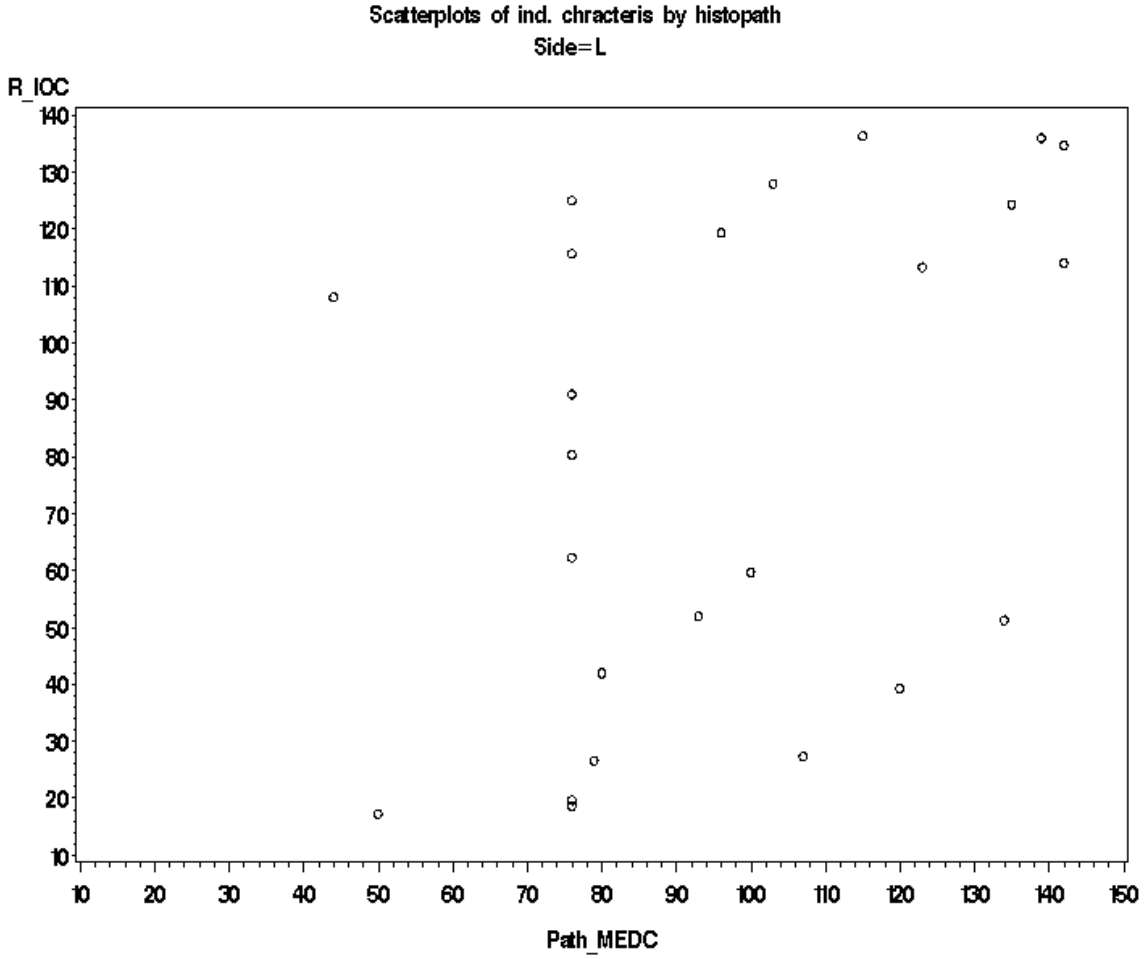
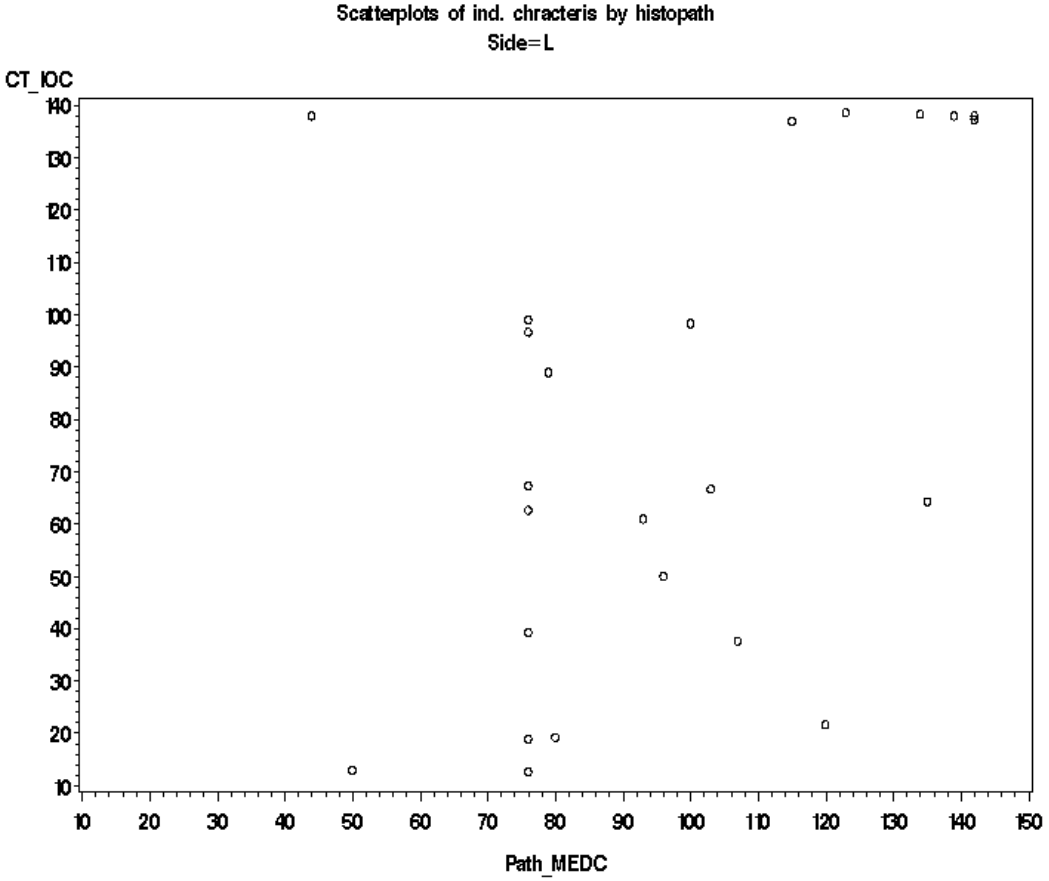


Figure 23. Scatter plot of CT increased opacity certainty (CT_IOC) compared to histopathology middle ear certainty (Path_MEDC) for the left side.



Discussion

We chose dogs that were scheduled to have TECA surgery for chronic external ear disease as our sample population because lateral bulla osteotomies are routinely included as part of this procedure at our hospital. This allowed us to remove imaging as a criterion for patient selection. Previous studies using CT and radiography suggest that otitis media is present with chronic external ear disease in approximately 52-62% of the canine cases when compared to surgical results. [56, 76] Therefore, we felt that the likelihood of finding concurrent middle ear disease in some of our dogs was high. This choice of sample population was also consistent with previous studies. [45, 56] Our population was predominantly Cocker Spaniels, with a wide age range and no sex predilection. It was interesting to note that approximately half of our population of dogs (48%) had bilateral external ear disease and approximately half of those cases (53%) had bilateral middle ear disease at surgery. This suggests that bilateral middle ear disease may be more prevalent than previously reported. [27] We chose to evaluate both bullae in each imaging study because this is common practice in the clinical setting. However, this may have resulted in a tendency to over or under estimate disease, especially when disease was bilateral. The presence of bilateral middle ear disease may make it more difficult for observers to use the contralateral bulla for a comparison when interpreting imaging studies.

An unexpected finding was that the side of involvement had an effect on diagnostic certainty and severity scores. This prevented us from being able to pool data from all ears for analysis. The most likely reason for this was that the severity of middle ear disease on the right side was consistently less than the left side in our sample population. We know of no explanation for why one ear side should have had a greater prevalence of disease.

Review of the medical records of the clinical cases in this study suggests the complications following surgery and culture results were comparable to previous results.[45, 46] The most common complications were incomplete or decreased palpebral reflex and facial nerve paresis or paralysis. Mild swelling associated with surgical site was also seen. The most common single isolate from culture was *Pseudomonas aeroginosa*. However, multiple cases had mixed culture results growing two or more organisms.

Surgical observations from this study were not as definitive as expected. One possible reason could be that the amount of exposure at surgery was considered poor to adequate in 41% of the cases. This may have limited our ability to accurately assess whether or not there was middle ear disease. Additionally, approximately one third of the samples submitted for histopathology yielded equivocal results. This reduced the number of bullae we could use for our analysis comparing the imaging modalities and histopathology. It was difficult in most cases to obtain the proper sample for histopathological analysis. Curettage of the bulla often provided shards of the bulla lining that were small and could easily be mixed with bone dust from drilling and other debris from the external ear. This was especially true when the lining appeared normal because of its thinness and adherence to the bulla wall. It is possible that more histopathologic samples from the middle ears would have been included if they were obtained by an osteotome or rongeurs, so that a larger piece of bulla wall could be obtained with the bulla lining intact. This would have provided the pathologist with better orientation and perhaps increased the level of diagnostic certainty for middle ear disease. The majority of the histopathologic samples that were examined contained evidence of inflammation. The fact that mild inflammation was found in a histological section from one of the clinically normal dogs indicates that mild otitis media may sometimes be subclinical. In future studies it may be helpful to establish a range of normal histopathologic changes that may be seen in bullae of clinically normal dogs. This could provide a better correlation between imaging and histopathology results.

There were 7 bullae from 6 dogs in which the surgical diagnosis of middle ear disease did not match the diagnosis from histopathology. All of these were considered to be negative for middle ear disease at surgery and positive on histopathology. In 4 of these cases, debris was seen in the middle ear at the time of surgery but the surgeon thought that the debris was introduced during removal of the external ear. It is possible that the debris was actually due to middle ear disease and that these cases should have been counted as surgical positives. However, there was no evidence of internal bone proliferation or thickening of the bulla lining to support the diagnosis of middle ear disease in these cases. The other 3 cases in the group had no evidence of debris or other changes to suggest middle ear disease at surgery. In all of the cases with a discrepancy between surgical and histopathologic diagnoses, the severity of disease found at histopathology was low ($\leq$ 55 on a scale to 150). Two of the 7 cases diagnosed as negative at surgery had a positive culture. This suggests that macroscopic evidence of middle ear inflammation may sometimes be undetectable at surgery. However, given the fact that one bulla of a clinically normal dog had evidence of inflammation on histopathology, perhaps a set of scoring criteria should be developed for histopathology of middle ear disease in which a normal range of inflammation could be defined.

Our diagnostic sensitivity results for radiography and CT were consistent with those obtained in a previous study that compared conventional radiography and CT to surgery. [56] Similar to the previous study, we provided readers with only transverse, hard-copy CT images. Providing readers with CT images in sagittal or dorsal (coronal) planes may have resulted in higher diagnostic certainty scores. As more veterinarians begin interpreting studies from computer monitors (soft-copy display), it will be important to also re-evaluate the effect of this change in methodology on observer diagnostic certainty. With soft-copy display, observers can change magnification, edge-enhancement and contrast/brightness settings as desired. In our study, the diagnostic sensitivity of CT was higher than the previously reported, but specificity was

approximately the same. It is possible that this increased sensitivity was due to the use of improved algorithms and thinner slices used in performing the CT studies. Sensitivity and specificity for radiography were slightly lower in our study than the previous study. When compared to surgery, there were two false positives for CT and 3 for radiography. The false positives were not the same for each modality. On CT, the false positives had a similar appearance at surgery and in imaging studies. At surgery, both cases had debris from the external ear canal protruding into the lateral aspect of the bulla. On the CT images of both cases, two of the observers saw increased opacity within the tympanic bulla just inside the tympanic membrane. The certainty and severity scores for these observers were consistent with disease but lower than usual. One observer saw no disease on both cases. One of the two cases was positive on histopathology and the other had an inadequate tissue sample to evaluate. It is possible with these cases that there was extension into the middle ear from the external ear and that surgery results should have been marked as abnormal. Another possibility is that the increased opacity seen by the two observers was material from the external ear that was extending into the middle ear. This is a common finding with extensive external ear disease and will continue to be a region that is difficult to assess correctly. Given the fact that there was mild inflammation on the histopathology sample of one of these cases, it would be advantageous to explore these bullae at surgery even though changes may not be seen. All three false positives for radiography were similar to those of CT in which two of the three observers saw increased opacity within the bulla but had low certainty and severity. One of these observers also saw changes in the bulla contour for two of the cases and bulla proliferation in the other. The other observer saw no disease. Histopathology was equivocal for two of the cases and positive for the other. At surgery, there was no evidence of middle ear disease for two of these cases. The other case had some debris within the bulla that was likely related to the external ear disease. It is possible that these false positives were caused by superimposition of overlying structures.

There were also false negatives when comparing radiography and CT to surgery. Computed tomography had 4 false negatives and radiography had 13. Three of the cases had false negatives for both modalities. All the false negative cases for CT had mild bulla lining thickening and 3 of the 4 had debris within the bulla at surgery. In 75% of the false negative cases seen with CT, at least one observer saw increased opacity within the bulla when the others did not. In the other case, two observers recorded evidence of bulla proliferation, but their certainty scores for middle ear disease were below the minimum limit we set for assigning a positive diagnosis. Perhaps the use of a narrower range of limiting values for our equivocal scores (acceptance of lower observer diagnostic certainty) would have resulted in larger sample numbers and higher sensitivities. All four CT negative cases had middle ear disease on histopathology. Of the 13 radiographic false negative cases, all had at least mild thickening of the bulla lining at surgery. Twelve of the 13 also had debris within the middle ear at surgery. Seven of the 13 cases were confirmed to have middle ear disease on histopathology. The other six cases were considered equivocal. These results indicate that radiography is less sensitive than CT for detecting bulla lining thickening and debris within the bulla cavity.

Neither CT nor radiography had a false positive when compared to histopathology. However, both had a high number of false negatives. All of the false negative cases had a severity score on histopathology that was less than 70 (scale 0 to 150). In fact, using an answer of “no middle ear disease” with CT or radiography predicted over 75% of the samples with a severity score less than 70. The cases that were not predicted by either modality had changes such as bulla proliferation and change in bulla contour, which may not be as evident on histopathology. For the most part, certainty scores at histopathology for these cases were also low. These results indicate that both CT and radiography are less sensitive for detecting disease when severity of middle ear disease is low. This interpretation is supported by the results of the paired T-Test. Certainty of the observers for disease in the middle ear was not consistent with histopathology certainty on the right

side for either modality. Evaluation of the bias plots show that severity of disease on the right side was lower than those on the left. This suggests that observer certainty was influenced by severity of the disease. The low severity of disease on the right side also had a bearing on the radiograph severity score. Radiographic severity scores were not consistent with histopathology severity scores for the right side as would be expected. Again, low degree of severity seemed to be the major contributing factor.

Correlation of individual characteristics of middle ear disease with histopathology was performed to see if any characteristics had a strong association with the histopathology results. A strong correlation between a particular imaging characteristic and histopathology would indicate that more weighting should be placed on the presence of that characteristic. Of all the imaging characteristics, only increased opacity within the bulla had a significant correlation with histopathology certainty for both modalities. This correlation was found only on the left side. A negative correlation was found on the right side, most likely due to the lower severity of middle ear disease on that side. However, evaluation of the scatter plots for certainty of increased opacity within the bulla on the left side revealed that there was no obvious trend of linearity (Figure 22-23). The positive correlation in these cases was therefore likely related to outlier cases. This indicates that certainty of increased opacity within the bulla had a stronger correlation with histopathology certainty than other criteria but the linear association was weak. The correlation was only strong when the severity was high. There were multiple criteria that had a strong correlation with histopathology severity. Correlation between histopathologic severity of middle ear disease and imaging estimates of severity for increased opacity within the bulla and bulla proliferation were statistically significant. Again, linearity on the scatter plots for these criteria was tentative and may have been affected by outlier cases (Figure 16-21). Lysis of the bulla was the only criterion that did not have a significant correlation with histopathologic severity for either modality. It is unclear why bulla bone lysis did not correlate with the histopathologic diagnosis of

middle ear disease. These correlation results indicate that both CT and radiography were better at predicting the severity of middle ear disease than the certainty. Findings indicate that all imaging characteristics except bulla lysis are good predictors of disease severity.

Another way to test the diagnostic validity of an imaging modality is to evaluate its consistency. We hypothesized that inter- observer variability would be lower with CT than radiography. We found that inter-rater variability for CT was indeed lower than radiography in certainty and severity scores of left ears. On the right side, however, variability for severity scores was lower with CT and variability for certainty scores was lower with radiography. One theory for this finding is that variability was affected by the lower overall disease severity seen on the right side. Lower severity of disease most likely decreased the observers' diagnostic certainty, which in turn resulted in increased inter- observer variance for CT. Some readers may have attributed more significance to subtle changes than others. Inter- observer variance for CT was lower than radiography in most of the criteria used to determine middle ear disease except for bulla proliferation (both certainty and severity) and increased opacity within the bulla (certainty only). Review of the individual scores for CT indicated that each observer interpreted the significance of abnormalities differently. This was most evident with bulla proliferation and increased opacity within the bulla. One observer consistently gave higher scores when bulla proliferation was present. This observer's perception of how thick the bulla wall should be and its characteristics were different from that used by the other two observers. Another observer gave consistently lower scores than the others when evaluating increased opacity within the bulla. Additional studies are needed to assess the effect that experience has on the interpretation of radiography and CT in dogs with suspected middle ear disease. We were not able to calculate observer experience effects because we did not have an equal number of cases in each severity category.

Overall, CT appeared to be more consistent than radiography in detecting changes that occur with middle ear disease. However, as severity of disease decreased, inter-observer variability increased for both modalities. It is possible that a lack of published reports correlating imaging characteristics with histopathologic findings affected observer confidence for diagnosing the more subtle cases. In future studies, providing readers with a list of imaging characteristics that have been found in dogs with histopathologic evidence of middle ear disease might help address this problem. Additionally, allowing access to soft-copy images may also help increase observer diagnostic certainty.

Currently at our hospital, lateral or ventral bulla osteotomy procedures are typically done along with the TECA procedure on chronic otitis externa cases, regardless of diagnostic imaging findings. Since both imaging modalities in our study had some false negatives, this common practice is somewhat validated. However, it is the author's opinion that pre-operative CT is still justified because it may provide important information about the extent and severity of the disease process that would alter the prognosis and choice of surgical exposure.

CONCLUSION

To our knowledge, this is the first prospective study that has compared findings from CT, radiography, surgery and histopathology in dogs with suspected middle ear disease. This is also the first study in which a visual analog scale method was used for quantifying certainty and severity of canine middle ear disease. Results of our study indicated that the diagnostic sensitivity of CT and radiography was higher for predicting canine middle ear disease when surgery was used as the gold standard versus when histopathology was used as the gold standard. Overall, CT was more sensitive and more specific than radiography for detecting middle ear disease when compared to surgical findings. When compared to histopathologic findings, CT was also more sensitive than and as specific as radiography. Inter- observer variability for CT was lower than radiography when severity of middle ear disease was moderate or high. Inter-observer variability was greater for CT than radiography when the severity of disease was low. The consistently low severity of the disease on the right side may have exacerbated the effect of observer disagreement on the significance of subtle changes. Observers were more likely to assign more variable significance to these changes, which produced more variability in the middle ear disease certainty scores. Inter- observer variability for scoring certainty and severity of most individual CT characteristics was very low. Inter-observer variability in assessing certainty and severity of bulla proliferation and certainty of increased opacity within the bulla was lower for radiography than CT. Review of the datasheets revealed that individual observers had conflicting scores for these criteria on CT. Correlation between certainty scores for imaging characteristics and histopathology was not as strong as that seen for severity scores. Certainty of increased opacity within the bulla was the only criterion that had a significant correlation with certainty of disease on histopathology. All imaging severity scores except bulla lysis appeared to correlate with histopathologic severity of middle ear disease.

Surgical candidates for TECA procedures were chosen as the sample population for the clinically-affected group because it is standard practice at our hospital to perform bulla osteotomies along with all TECA procedures, regardless of the results of imaging studies. The breed, age, and gender distribution of our sample population was consistent with that used in previous studies comparing surgical and imaging results in dogs with suspected middle ear disease. Imaging techniques used in our study were similar to those currently being used at most veterinary referral centers. The author supervised all imaging studies and surgical biopsies to help minimize variation. Some variation in tissue collection techniques may have occurred because different surgeons performed the surgeries. The same board-certified veterinary pathologist evaluated all histopathology samples. Three veterinary radiologists (two board-certified and 1 resident-in-training) evaluated the images independently and in random order, without knowledge of surgical or histopathologic findings.

In summary, the results of this study justify the use of CT as a pre-operative imaging technique for assessing extent and severity of middle ear disease in dogs with severe, chronic otitis externa. However, there are limitations that should be taken into consideration when interpreting the results. Different observers may interpret the significance of CT abnormalities differently when middle ear disease severity is low. This increase in inter-observer variance may also cause the accuracy and reliability of CT for detecting disease to be reduced. Also, there is a chance that CT results could be negative when there is histopathologic evidence of middle ear disease. Histopathologic evidence of middle ear disease can also be present when there is no gross evidence of middle ear disease at surgery. Future studies are needed to assess the effects of hard-copy versus soft-copy image display and the use of CT reformatting on observer diagnostic certainty. The effect of providing observers with examples of known cases with mild, moderate, and severe middle ear disease also needs to be examined. Improved methods for obtaining high diagnostic quality surgical biopsies from tympanic bullae

should be developed. A normal reference range for histopathologic characteristics of canine middle ear tissue should also be established.

BIBLIOGRAPHY

1. Evans HE. The Ear In: Evans HE, Miller ME, eds. *Miller's anatomy of the dog*. 3rd ed. Philadelphia: W.B. Saunders, 1993; 988-1008.

2. Reece WO. The Sensory Organs In: Reece WO, ed. *Physiology of domestic animals*. Philadelphia: Lea & Febiger, 1991; 32-63.

3. Neer T. Otitis Media. *Compend Contin Educ Pract Vet* 1982; 4:410-417.

4. Wakuri H, Mori S, Mutoh K, et al. Fiber arrangement in the canine tympanic membrane. *Okajimas Folia Anat Jpn* 1988; 65:11-17.

5. Stern-Bertholtz W, Sjostrom L, Hakanson NW. Primary secretory otitis media in the Cavalier King Charles spaniel: a review of 61 cases. *J Small Anim Pract* 2003; 44:253-256.

6. Edwards DF, Patton CS, Kennedy JR. Primary ciliary dyskinesia in the dog. *Probl Vet Med* 1992; 4:291-319.

7. Grono LR. Observations on the incidence of otitis externa in the dog. *Aust Vet J* 1969; 45:417-419.

8. Holzworth J. Naturally occurring upper respiratory infection in cats. *J Am Vet Med Assoc* 1971; 158:Suppl 2:964-968.

9. Gregory SP. Middle ear disease associated with congenital palatine defects in seven dogs and one cat. *J Small Anim Pract* 2000; 41:398-401.

10. Rosychuck R, Luttgen P. Diseases of the ear In: Ettinger SJ, Feldman EC, eds. *Textbook of veterinary internal medicine: diseases of the dog and cat.* 5th ed. Philadelphia: W.B. Saunders Co., 2000; 986-1001.

11. Little CJ, Pearson GR, Lane JG. Neoplasia involving the middle ear cavity of dogs. *Vet Rec* 1989; 124:54-57.

12. Stone HE, Lipa M, Bell RD. Primary adenocarcinoma of the middle ear. *Arch Otolaryngol* 1975; 101:702-705.

13. Harrison K, Cronin J, Greenwood N. Ceruminous adenocarcinoma arising in the middle ear. *J Laryngol Otol* 1974; 88:363-368.

14. Strafuss AC. Sebaceous gland adenomas in dogs. *J Am Vet Med Assoc* 1976; 169:640-642.

15. Strafuss AC. Sebaceous gland carcinoma in dogs. *J Am Vet Med Assoc* 1976; 169:325-326.

16. Kirpensteijn J. Aural neoplasms. *Semin Vet Med Surg (Small Anim)* 1993; 8:17-23.

17. Goldschmidt MH. Basal- and squamous-cell neoplasms of dogs and cats. *Am J Dermatopathol* 1984; 6:199-206.

18. Strafuss AC, Cook JE, Smith JE. Squamous cell carcinoma in dogs. *J Am Vet Med Assoc* 1976; 168:425-427.

19. Bichsel P, Scharer V. [A neoplasm of the middle ear causing a vestibular syndrome in a dog]. *Schweiz Arch Tierheilkd* 1985; 127:717-722.

20. Pratschke KM. Inflammatory polyps of the middle ear in 5 dogs. *Vet Surg* 2003; 32:292-296.

21. Harvey CE, Goldschmidt MH. Inflammatory polypoid growths in the ear canal of cats. *J Small Anim Pract* 1978; 19:669-677.

22. Rogers KS. Tumors of the ear canal. *Vet Clin North Am Small Anim Pract* 1988; 18:859-868.

23. Seim HB, 3rd. Middle ear In: Slatter DH, ed. *Textbook of small animal surgery*. Philadelphia: W.B. Saunders, 1985; 1568-1576.

24. Little CJ, Lane JG, Gibbs C, et al. Inflammatory middle ear disease of the dog: the clinical and pathological features of cholesteatoma, a complication of otitis media. *Vet Rec* 1991; 128:319-322.

25. Wright CG, Meyerhoff WL. Pathology of otitis media. *Ann Otol Rhinol Laryngol Suppl* 1994; 163:24-26.

26. Little CJ, Lane JG, Pearson GR. Inflammatory middle ear disease of the dog: the pathology of otitis media. *Vet Rec* 1991; 128:293-296.

27. Shell LG. Otitis media and otitis interna. Etiology, diagnosis, and medical management. *Vet Clin North Am Small Anim Pract* 1988; 18:885-899.

28. Bruyette DS, Lorenz MD. Otitis externa and otitis media: diagnostic and medical aspects. *Semin Vet Med Surg (Small Anim)* 1993; 8:3-9.

29. Hellstrom S, Eriksson PO, Yoon YJ, et al. Interactions between the middle ear and the inner ear: bacterial products. *Ann N Y Acad Sci* 1997; 830:110-119.

30. Juhn SK, Jung TT, Lin J, et al. Effects of inflammatory mediators on middle ear pathology and on inner ear function. *Ann N Y Acad Sci* 1997; 830:130-142.

31. Spangler EA, Dewey CW. Meningoencephalitis secondary to bacterial otitis media/interna in a dog. *J Am Anim Hosp Assoc* 2000; 36:239-243.

32. Shilton CM, Thompson MS, Meisner R, et al. Nasopharyngeal myxosarcoma in a Bengal tiger (Panthera tigris). *J Zoo Wildl Med* 2002; 33:371-377.

33. Harlizius J, Kluczniok C, Bollwahn W. Radiographic imaging of otitis media and interna in pigs. *Vet Radiol Ultrasound* 1997; 38:421-423.

34. Trevor PB, Martin RA. Tympanic bulla osteotomy for treatment of middle-ear disease in cats: 19 cases (1984-1991). *J Am Vet Med Assoc* 1993; 202:123-128.

35. Sade J. Middle ear mucosa. *Arch Otolaryngol* 1966; 84:137-143.

36. Chole RA. The molecular biology of bone resorption due to chronic otitis media. *Ann N Y Acad Sci* 1997; 830:95-109.

37. Ziemer LS, Schwarz T, Sullivan M. Otolithiasis in three dogs. *Vet Radiol Ultrasound* 2003; 44:28-31.

38. Fergie JE, Purcell K. The role of inflammatory mediators and anti-inflammatory drugs in otitis media. *Pediatr Ann* 1998; 27:76-81.

39. Cox CL, Slack RW, Cox GJ. Insertion of a transtympanic ventilation tube for the treatment of otitis media with effusion. *J Small Anim Pract* 1989; 30:517-519.

40. Boothe HW, Jr. Surgical management of otitis media and otitis interna. *Vet Clin North Am Small Anim Pract* 1988; 18:901-911.

41. Boothe HW. Surgery of the tympanic bulla (otitis media and nasopharyngeal polyps). *Probl Vet Med* 1991; 3:254-269.

42. Rose WR. Small animal clinical otology. Necropsy --2. Pathology of middle ear and biopsy. *Vet Med Small Anim Clin* 1978; 73:764-767.

43. Boothe HW. Middle ear- bulla osteotomy In: Bojrab MJ, Birchard SJ, Tomlinson JL, eds. *Current techniques in small animal surgery*. 3rd ed. Philadelphia: Lea & Febiger, 1990; 147-150.

44. Smeak DD, Kerpsack SJ. Total ear canal ablation and lateral bulla osteotomy for management of end-stage otitis. *Semin Vet Med Surg (Small Anim)* 1993; 8:30-41.

45. Mason LK, Harvey CE, Orsher RJ. Total ear canal ablation combined with lateral bulla osteotomy for end-stage otitis in dogs. Results in thirty dogs. *Vet Surg* 1988; 17:263-268.

46. Beckman SL, Henry WB, Jr., Cechner P. Total ear canal ablation combining bulla osteotomy and curettage in dogs with chronic otitis externa and media. *J Am Vet Med Assoc* 1990; 196:84-90.

47. Smeak DD, Crocker CB, Birchard SJ. Treatment of recurrent otitis media that developed after total ear canal ablation and lateral bulla osteotomy in dogs: nine cases (1986-1994). *J Am Vet Med Assoc* 1996; 209:937-942.

48. Devitt CM, Seim HB, 3rd, Willer R, et al. Passive drainage versus primary closure after total ear canal ablation-lateral bulla osteotomy in dogs: 59 dogs (1985-1995). *Vet Surg* 1997; 26:210-216.

49. Denny HR. The results of surgical treatment of otitis media and interna in the dog. *J Small Anim Pract* 1973; 14:585-600.

50. Sharp NJ. Chronic otitis externa and otitis media treated by total ear canal ablation and ventral bulla osteotomy in thirteen dogs. *Vet Surg* 1990; 19:162-166.

51. McAnulty JF, Hattel A, Harvey CE. Wound healing and brain stem auditory evoked potentials after experimental total ear canal ablation with lateral tympanic bulla osteotomy in dogs. *Vet Surg* 1995; 24:1-8.

52. Hoskinson JJ. Imaging techniques in the diagnosis of middle ear disease. *Semin Vet Med Surg (Small Anim)* 1993; 8:10-16.

53. Garosi LS, Dennis R, Schwarz T. Review of diagnostic imaging of ear diseases in the dog and cat. *Vet Radiol Ultrasound* 2003; 44:137-146.

54. Myers W. Cranial vault and associated structures In: Thrall DE, ed. *Textbook of veterinary diagnostic radiology*. 3rd ed. Philadelphia: W.B. Saunders, 1998; 59-65.

55. Remedios A, Fowler J, Pharr J. A comparison of radiographic versus surgical diagnosis of otitis media. *J Am Anim Hosp Assoc* 1991; 27:183-188.

56. Love N, Kramer R, Spodnick G, et al. Radiographic and computed tomographic evaluation of otitis media in the dog. *Vet Radiol Ultrasound* 1995; 36:375-379.

57. Russo M, Covelli EM, Meomartino L, et al. Computed tomographic anatomy of the canine inner and middle ear. *Vet Radiol Ultrasound* 2002; 43:22-26.

58. Barthez P, Koblik P, Hornof W, et al. Apparent Wall Thickening in Fluid Filled Versus Air Filled Tympanic Bulla in Computed Tomography. *Vet Radiol Ultrasound* 1996; 37:95-98.

59. Dickie AM, Doust R, Cromarty L, et al. Comparison of ultrasonography, radiography and a single computed tomography slice for the identification of fluid within the canine tympanic bulla. *Res Vet Sci* 2003; 75:209-216.

60. Maroldi R, Farina D, Palvarini L, et al. Computed tomography and magnetic resonance imaging of pathologic conditions of the middle ear. *Eur J Radiol* 2001; 40:78-93.

61. Veillon F, Riehm S, Roedlich MN, et al. Imaging of middle ear pathology. *Semin Roentgenol* 2000; 35:2-11.

62. Allgoewer I, Lucas S, Schmitz SA. Magnetic resonance imaging of the normal and diseased feline middle ear. *Vet Radiol Ultrasound* 2000; 41:413-418.

63. Forrest LJ. The head: excluding the brain and orbit. *Clin Tech Small Anim Pract* 1999; 14:170-176.

64. Garosi LS, Dennis R, Penderis J, et al. Results of magnetic resonance imaging in dogs with vestibular disorders: 85 cases (1996-1999). *J Am Vet Med Assoc* 2001; 218:385-391.

65. Garosi LS, Lamb CR, Targett MP. MRI findings in a dog with otitis media and suspected otitis interna. *Vet Rec* 2000; 146:501-502.

66. Brunner E, Turk R, Swoboda H, et al. [Significance of computerized tomography in middle ear diagnosis]. *Laryngol Rhinol Otol (Stuttg)* 1986; 65:327-330.

67. Koltai PJ, Eames FA, Parnes SM, et al. Comparison of computed tomography and magnetic resonance imaging in chronic otitis media with cholesteatoma. *Arch Otolaryngol Head Neck Surg* 1989; 115:1231-1233.

68. Dickie AM, Doust R, Cromarty L, et al. Ultrasound imaging of the canine tympanic bulla. *Res Vet Sci* 2003; 75:121-126.

69. Tuomanen EI. Pathogenesis of pneumococcal inflammation: otitis media. *Vaccine* 2001; 19:S38-S40.

70. St Geme JW. The pathogenesis of nontypable *Haemophilus influenzae* otitis media. *Vaccine* 2001; 19:S41-S50.

71. Mogi G, Suzuki M. The role of IgE-mediated immunity in otitis media: fact or fiction? *Ann N Y Acad Sci* 1997; 830:61-69.

72. Schousboe LP, Ovesen T, Pedersen CB. Middle ear epithelium has inflammatory capacity. *Acta Otolaryngol Suppl* 2000; 543:89-91.

73. Wielinga EW, Peters TA, Tonnaer EL, et al. Middle ear effusions and structure of the tympanic membrane. *Laryngoscope* 2001; 111:90-95.

74. Angus JC, Lichtensteiger C, Campbell KL, et al. Breed variations in histopathologic features of chronic severe otitis externa in dogs: 80 cases (1995-2001). *J Am Vet Med Assoc* 2002; 221:1000-1006.

75. Feeney DA, Fletcher TF, Hardy RM. *Atlas of correlative imaging anatomy of the normal dog: ultrasound and computed tomography*. Philadelphia: Saunders, 1991.

76. Spruell JS. Treatment of otitis media in the dog. *J Small Anim Pract* 1964; 5:107-122.

VITA

Jacob John Rohleder was born (12/28/1969) and raised in Jasper, Indiana. He is the son of Joe Rohleder, a retired high school teacher and coach, and his wife Judy, an antique dealer and small business owner. Joe and Judy currently live in a restored stagecoach stop in Jasper, Indiana. Other family members include a brother Jay, his wife Vicki and their children (Gabe, Sophie, Isaac, and Elijah) and a sister Jan and her husband Tom.

After high school, Jacob attended Purdue University in which he received his undergraduate degree in Biological Sciences in 1992. Jacob then went to work at the Krannert Institute of Cardiology in Indianapolis, Indiana for two years where he served as a senior research assistant. In 1994, Jacob was accepted into the school of veterinary medicine at Purdue University to complete his doctorate degree. He graduated in 1998. After graduation Jacob was accepted into a one year small animal surgery and medicine internship at Metropolitan Veterinary Hospital in Akron, Ohio. Jacob then moved back to Indianapolis, Indiana were he worked as an emergency Veterinarian from 1999-2000. In 2000 Jacob accepted a residency in radiology at the Virginia-Maryland Regional College of Veterinary Medicine in Blacksburg, Virginia where he currently resides.

Jacob enjoys art, movies, sports and traveling. Other hobbies include hiking, bicycle riding and various other outdoor activities.