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In this study, we used five tumor models namely : Nude mice implanted with canine malignant melanoma (MM), mast cell tumor (MCT), mammary adenocarcinoma (MAC), malignant synovioma (MS), and osteosarcoma (OS). To evaluate the incidence of radiation-induced apoptosis *in vitro*, tumor tissues from each model were cultured and irradiated (0, 4, 16 Gy of X-rays). Apoptotic cells in the irradiated tissues were detected, using the TUNEL method at 2, 4, 6, and 12 hours after irradiation. To evaluate the radiocurability of each tumor *in vivo*, implanted tumors in nude mice were irradiated at 48 Gy administered in 4 Gy fractions over 4 weeks and their growth rates were monitored individually.

The incidence of radiation-induced apoptosis *in vitro* from highest to lowest incidence are : MCT (22% by 4 Gy at 12 hours), MAC (11%), MM and OS (5%), and MS (2%).

The radiocurability of tumors *in vivo* are : MCT showed the highest radiocurability as CR (Complete Response) 4/4, followed by MAC as MR (Minimum Response) 4/4. MM showed lower as CR1, MR1 and PD (Progress Disease) 2/4, OS and MS showed the lowest radiocurability as CR1 and PD4/5, PD5/5 respectively.

These results suggest that the tumors with many apoptotic cells in the irradiated tissue *in vitro* showed higher radiocurability *in vivo*. The efficient detection of radiation-induced apoptotic cells *in vitro* from the various X-ray exposure conditions in this study was at 4 Gy of X-ray exposure and 12 hours apoptosis-developing time post-irradiation.

In conclusion, the detection of radiation-induced apoptosis in this study could be used as a predictive assay for radiotherapy of the five models used, and could be adopted to other canine tumors.

### Efficacy of atrial natriuretic peptide administration in dogs with chronic heart failure caused by experimentally induced mitral regurgitation

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Atrial natriuretic peptide (ANP) is a cardiac hormone which is responsible for the regulation of blood pressure and body fluid homeostasis. Recently, the clinical application of recombinant human  $\alpha$ -ANP (carperitide : HANP<sup>®</sup>) is possible in human acute heart failure cases. The objective of this study is to evaluate the efficacy of carperitide in the treatment for canine mitral regurgitation which occurs frequently in canine acquired heart diseases.

Chronic mitral regurgitation (MR) was experimentally induced in six dogs by the rupture of

mitral valvular chordae tendineae. Two weeks after that, the time courses of the hemodynamics, diuresis, natriuresis and plasma ANP levels were compared during the continuous administration of different carperitide doses (0.1, 0.5 and 1  $\mu$ g/kg/min) for 1 hour and 1 hour after the withdrawl.

The plasma ANP levels and the pulmonary arterial wedge pressure (PAWP) increased after the induction of MR and a good correlation was evident ( $r=0.85$ ). The heart rate, the mean arterial pressure, the PAWP and the double

product, as an indicator of myocardial oxygen consumption, decreased during and after the administration of carperitide in all dogs. The PAWP was remarkably reduced and the cardiac output increased during and after the administration of carperitide in the three dogs with overt CHF (CHF+) among them in comparison with the other three dogs without CHF (CHF-). But the urine volume and the excretion of sodium increased during and after the infusion of carper-

itide in the CHF- dogs, compared with the CHF+ dogs. On the relationship between PAWP and cardiac index, all plots of the CHF+ dogs shifted upward and to left, meaning an improvement in cardiac function, during and after the injection of carperitide. In contrast, all plots of the CHF- dogs showed little change.

In conclusion, it was suggested that carperitide is effective in the treatment for dogs with CHF caused by chronic mitral regurgitation.

### Measurement of keratan sulfate in sera and synovial fluid from horses by a monoclonal antibody 1/14/16H9 reacting with equine keratan sulfate

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The inhibition-ELISA for the measurement of equine keratan sulfate (KS) concentration was established by using an equine KS monoclonal antibody 1/14/16H9, and the usefulness of 1/14/16H9 monoclonal antibody was evaluated for this purpose.

An inhibition-ELISA using 1/14/16H9 antibody for determination of KS was optimized. The sensitivity of the assay could be substantially improved by increasing the dilution of primary antibody (1/14/16H9, 1:25,000), and the binding was detected by a peroxidase-conjugated antibody (second antibody, 1: 2,500). Precision data were obtained over the range 39–319 ng/ml of KS concentration in this assay.

KS concentration were measured in sera from foals (from 1 week after birth to the age of 5 months), and sera and synovial fluids from horses which were experimentally induced arthritis by the injection of chymopapain (30 mg/joint) into the carpal joint. The KS concentration in these samples were also evaluated by using 1/20/5D4

antibody.

In this assay system, serum and synovial fluid samples were diluted as follows; sera of foals: 20–40 times, sera of arthritic horses: 1–2 times, and synovial fluids: 100–800 times.

In the sera, values of 1/20/5D4 monoclonal antibody were significantly higher than that of 1/14/16H9 monoclonal antibody ( $p < 0.01$ ). In synovial fluids, no statistical difference was found between the values by using both monoclonal antibodies. The values of samples in the arthritic horses measured by both antibodies showed similar fluctuations.

In sera, there was a close correlation between the values measured by both antibodies in 3–14 days after injection of chymopapain, while no obvious correlation was found in 0–3 and 14–49 days. In synovial fluids, the correlation index was low in 3–17 days, while a close correlation was detected in 0–3 days and 17–31 days after injection of chymopapain.

These results show that 1/14/16H9 antibody