

Development of a Large Animal Canine Model of Stroke: How a Skull Base Approach and Indocyanine Green Angiography Improve Consistency and Decrease Mortality

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Introduction

Stroke remains a colossal problem worldwide. Despite the advances in medical technology only 4% of strokes are treated, making it the fourth leading cause of death. Several round table discussions have been held with industry leaders and consistently it has been recommended that large animal stroke studies are needed to evaluate new treatments.

Methods

Twenty adult male Beagles where used in our study. We compared endovascular, combined endovascular/surgical and purely surgical methods for developing our model. A surgical approach modified from Yanaka et al, 1996 was used. Briefly, a pterional craniotomy is performed with drilling of the temporal floor, minimizing retraction on the temporal lobe. The azygous ACA is identified and clipped. The MCA is then identified and coagulated and cut distal to the lenticulostriate vessels. Using indocyanine green we then identify collateral blood flow to the distal MCA which is then occluded through vessel coagulation. After one hour the aneurysm clip is removed and the animals recovered. Neurological examination is then performed



based on a modified protocol from Boulus et al.

Results

Our current approach has now been validated in our last 6 animals with no mortality. Stroke is seen on MRI at 24 hours with an average volume of 1469.5 \pm 173.62 mm3. This remains stable at one week. The average stroke volume determined histologically at one month is 1763.1 \pm 16.8 mm3. Neurological exam consistently demonstrates left sided weakness, neglect, and circling, falling to the left and unstable gait. While weakness improves in some animals the remainder of deficits are persistent in all animals. Average neurological score at 24 hours and one week are 25 \pm 3.6

and 18.75±7.9 respectively.



ICG Injection

	e Stroke Clinical Assessment Rating Scale		Proprioceptive Positioning (Invert pave placing dorsal surface in contact with	h ground - dog should immediately place foot in normal position)
Dog ED Number:	Age:	Date of Testing	Right kongaw	2 = servene delay 1 = moderate delay 0 = normal
Assessment Parameter	Rating	Score	Left foregow	2 * sarvere delay 1 * moderate delay 0 * normal
Careballar Atoxia	Dr normal stance 3 = severe gait dysmetria 2 = moderae gait dysmetria		Right Ningham	2 = severe delay 1 = moderate delay 0 = normal
	1 = modeol gait dynimetria 0 = normal gait		Left Ninger	2 = severe delay 1 = moderate delay 0 = normal
Leaning and Falling to One Side	3 = severe learning and falling to one side 2 = moderate learning and falling to one side 1 = moderat learning and falling to one side		Placing Response (non-visual) Cover dog's eye, pick up animal and move it to	mards edge of a table. When paw touches table edge it should refinily place pa
	0 = no learning and failing		Right Arregion	1 = no response 0 = nomue response
Head Tit	3 = severe head SR 2 = moderate head SR 1 = modest head SR		Latt tangan	1 * no response 0 * normá response
	0 = no head th		 (Clame procedure as non-visual task, but eyes remain open. Dog should reflexly extend paw on to table surface before touching or 	
Nystagmus	2 = moderate nyslagmus 1 = moderate nyslagmus		Right Empire	1 = no reporte 0 = normal response
Dilatoral Mantibular Almaia	E = no nyetagenze		Latterspan	0 = normal response
(Exhibits sole-to-sole head movements, reluctant to move, maintains projubed position)	2 - moderate 1 - moderat 8 - norm		Transr	3 * srupre 2 * moderate 1 * moderat 0 * none
Neniperesis	Br severs 2 = mailerate 1 = mailerate		Auditory Response	1 • no response to noise 0 • normal orientation to noise
	8 = none		Auditory Response (psilateral side)	Inno response Omorrial orientation
Paraparesis	2 + moderate 2 + moderate 1 = moder		Auditory Response (contralateral side)	t-no response O-normal orientation
			Beel Andralation Attempt	Inter-statement Provide to right self bud riskes Oriside to right self Forstable to right self Angenetis and angenetismen Angenetisment Provides Units to sale Provides Units to sale Provides Units to sale Provides Originational
			Vocalization	2-rome T-homosignunts D-normal
			Consciousness	Britises not assalan 2-assalans ar recipus stimulus 1-assalans ar monoral stimulation
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Conclusions

We have developed a highly consistent and predictable large animal canine stroke model with very low mortality.

References

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