

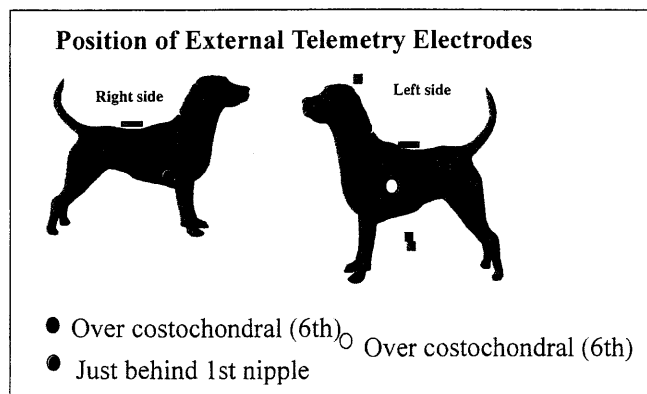
Benefits and limitations of an external telemetry system on canine toxicity studies

K. MOYSER, J. SCHOFIELD, D. SIMPSON and D. HUNTER

- Historically, physiological monitoring on canine toxicity studies has been limited to recording a conventional electrocardiogram (ECG) and systemic arterial blood pressure (ABP; invasively or non-invasively).
- Measurements, therefore, are restricted by practical limitations to "snap-shot" recordings (aimed at Cmax), leaving gaps when changes in physiological parameters, particularly ECG, could go undetected.
- To investigate this further, an external telemetry system, supplied by EMKA Technologies, was used to record a single lead ECG for a 24 post-dose period combined with a conventional 4 lead ECG and direct ABP to provide additional information at specific time points.
- Two compounds were used, an endothelin receptor antagonist (compound A) and a potassium channel opener (compound B), to examine the profile of any ECG changes, from two very different classes of drug.

Single dose investigative study in the dog

- Compound A – endothelin A receptor antagonist
- Compound B – potassium channel opener
- n=2 per compound (females)
- Preliminary assessment of biochemical changes predictive of arteritis
- Animals acclimatized to recording jackets during pre-test period
- Conventionally recorded ECG (cardiac intervals), pre-test and day 1 post-dose (1 or 4 hours; compound B & A respectively)
- Compared to external telemetry (EMKA) baseline recordings and 24 hour continuous monitoring on day 1



Conventional vs telemetry ECG data
Animal 1 & 2 – Compound A

Parameter	Conventional ECG			Telemetry ECG		
	Pre-Test	Day 1, Pre-Dose	Day 1, +4 Hours	Pre-Test	Day 1, Pre-Dose	Day 1, +4 Hours
Heart rate	136	112	128	102	147	126
PR interval	93	97	91	104	93	88
QRS duration	53	53	52	44	43	44
QT interval	186	179	183	186	137	177
QTcP	244	230	236	224	227	229
Arterial BP	115/65	130/75	100/90	NA		

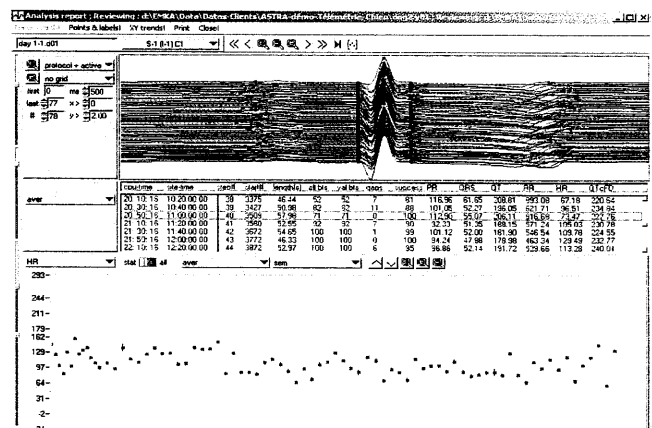
Heart rate	164	112	116	89	111	87
PR interval	105	107	109	116	109	117
QRS duration	52	54	55	45	42	51
QT interval	166	187	185	198	176	218
QTcP	232	230	230	228	218	250
Arterial BP	125/75	175/100	145/75	NA		

Conventional vs telemetry ECG data
Animal 3 & 4 – Compound B

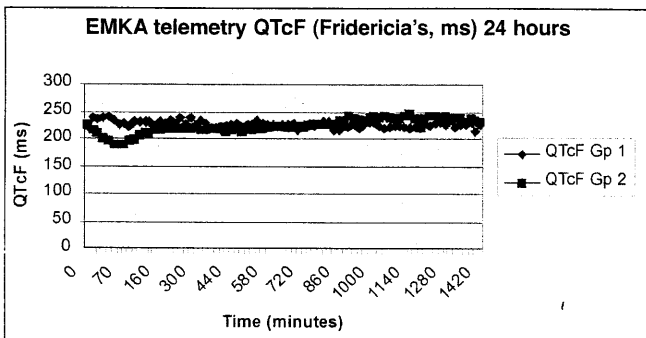
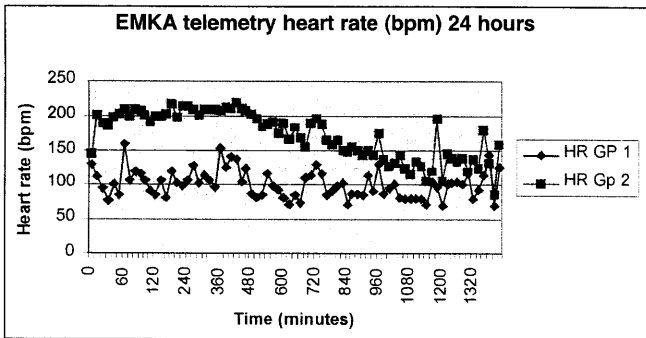
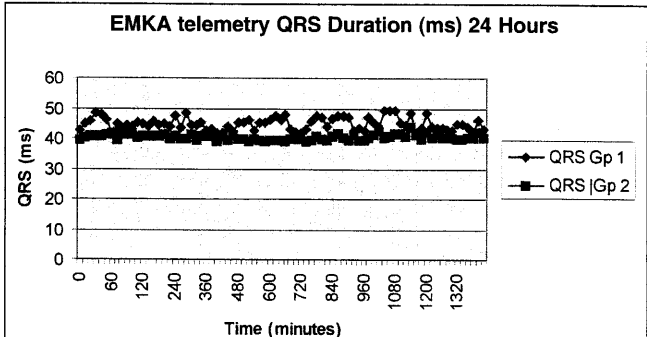
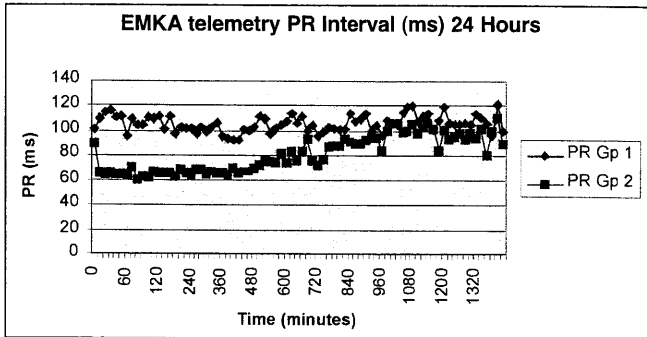
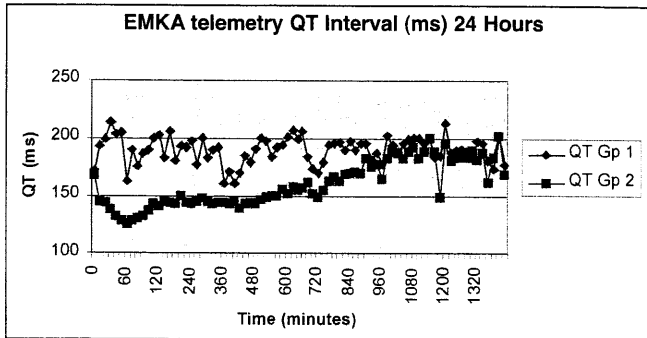
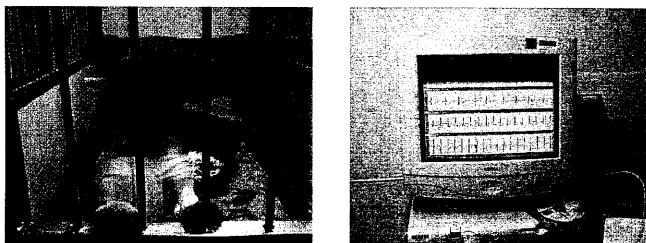
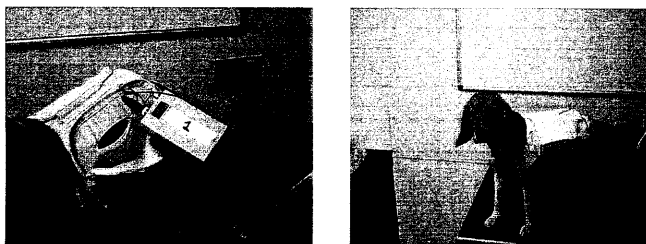
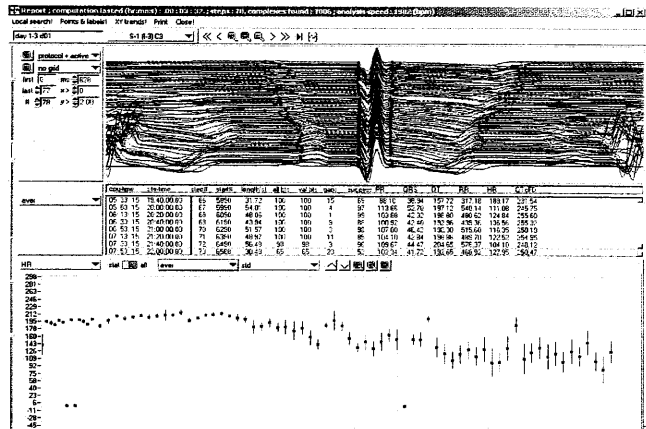
Parameter	Conventional ECG			Telemetry ECG		
	Pre-Test	Day 1, Pre-Dose	Day 1, +4 Hours	Pre-Test	Day 1, Pre-Dose	Day 1, +4 Hours
Heart rate	160	124	208	96	141	199
PR interval	105	112	69	111	96	66
QRS duration	49	50	51	44	41	42
QT interval	171	179	135	186	167	122
QTcP	237	228	204	221	233	183
Arterial BP	110/65	115/60	85/35	NA		

Heart rate	112	100	228	85	148	219
PR interval	93	97	60	92	84	62
QRS duration	50	51	52	42	39	42
QT interval	194	206	143	198	169	128
QTcP	239	244	223	225	229	197
Arterial BP	120/75	125/75	65/35	NA		

Heart rate Dog 1 (A) Day 1, 24hrs



Heart rate Dog 3 (B) Day 1, 24hrs



Possible advantages and disadvantages of an external telemetry system

- Advantages:
- Continuous ECG monitoring
 - Non-invasive
 - Relatively cheap (re-useable transmitters)
 - Technically simple
 - User-friendly software (GLP compliant; ER/ES)
 - Extensive analysis available (trend and stats analysis)
 - Measurements appear to be accurate, making the data reliable!
- Disadvantages:
- Excessive data could be produced on larger toxicity studies
 - No BP (although an invasive option will be available)
 - Some additional resource required (GTO buy-in important)
 - Over interpretation (spontaneously arrhythmias) will need consideration
 - Adaptation for specific toxicity study design will be needed (including animal units/occupation)