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Use of the emka Technologies System for ECG Assessments on Toxicology Studies

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Introduction

Inclusion of ECGs in toxicology studies has conventionally been at 'snap-shot' time-points, with the analysis of ECGs limited to a small number of complexes. Improving the quality and quantity of the waveforms assessed on toxicology studies will enable improved decision-making and add value to the design of subsequent cardiovascular safety pharmacology studies.

Objective

To conduct a feasibility study of automating the capture and analysis of ECGs on toxicology studies using the emka data acquisition/analysis system. The key objective is to define the resource implications of ECG capture to reporting using the traditional methods of paper traces versus automated analysis.

Study Design

Six male and 6 female beagle dogs (Harlan UK) had 2 sets of external skin ECG electrodes to record lead I, II, III, aVL, aVR and aVF. One set was attached to the emka data acquisition and analysis system, the other set was attached to a Nihon Koden Electrocardiograph (Cardiofax ECG-9620).

ECGs were acquired simultaneously using both systems at predose and at 1h and 5h post dose.

All animals were orally dosed by gavage with Control on Day 1 and then 3 animals/sex were dosed with either 4mg/kg or 16 mg/kg Sotalol (p.o.) at 1-2 day intervals.

All data was 100% checked with, whenever possible, the same ECG complexes measured for both systems.

This pharmacological validation supported the validation of the emka system.

Acceptance Criterion

Acceptance criterion for this comparison is 5% between both systems for all parameters.

Potential differences were due to:

- Slightly different lead position
- Different hardware/software
- Sampling frequency
- Accuracy limitations of measurements on paper

Results

- Good correlation between data from emka and traditional methods for all parameters (HR and all lead II ECG parameters)
- Data for all parameters within acceptance criterion
- Peak QTC effects (% increase with 9 mg/kg sotalol vs control)

			ECG Intervals					
			PR (ms)			QRS (ms)		
			Vehicle	4 mg/kg	16 mg/kg	Vehicle	4 mg/kg	16 mg/kg
Predose	Male	emka	107	94	109	45	43	40
		Paper	105	92	107	43	42	40
	Female	emka	100	110	97	42	44	42
		Paper	103	108	98	40	42	41
+1h	Male	emka	106	106	123	46	48	44
		Paper	105	108	121	47	48	43
	Female	emka	103	123	112	42	45	46
		Paper	103	129	113	42	44	47
+5h	Male	emka	96	105	116	42	49	45
		Paper	96	109	112	41	48	46
	Female	emka	98	122	117	42	48	45
		Paper	99	125	120	43	49	45

Table 1

			ECG Intervals					
			QT (ms)			HR (bpm)		
			Vehicle	4 mg/kg	16 mg/kg	Vehicle	4 mg/kg	16 mg/kg
Predose	Male	emka	191	199	186	122	118	122
		Paper	190	197	186	119	113	130
	Female	emka	188	193	188	130	121	119
		Paper	182	190	180	130	122	126
+1h	Male	emka	201	215	218	112	98	81
		Paper	197	209	217	112	104	82
	Female	emka	194	223	226	120	81	89
		Paper	192	227	225	120	79	92
+5h	Male	emka	193	222	204	127	95	93
		Paper	191	223	204	129	89	97
	Female	emka	188	199	221	127	111	87
		Paper	187	207	225	133	103	83

Table 2

Conclusion

Use of a data acquisition and analysis system (emka) provides an improved method of measuring toxicology ECGs in comparison to traditional methods.

- Technically simple to validate and use
- No impact on the efficiency of running physiology sessions on toxicology studies
- FDA 21 CFR Part 11 compliant system
- Increased speed of data reporting - with more options available
- Availability of critical data on test items to speed up the decision making process
- Additional information for subsequent Safety Pharmacology CV studies
- Higher quality ECG waveforms
- Visibility of all leads at one time on one screen
- Ability to analyse more ECG complexes
- The outcome of this feasibility study demonstrates that this method of ECG capture and analysis provides "added value" to "traditional type" toxicology studies.

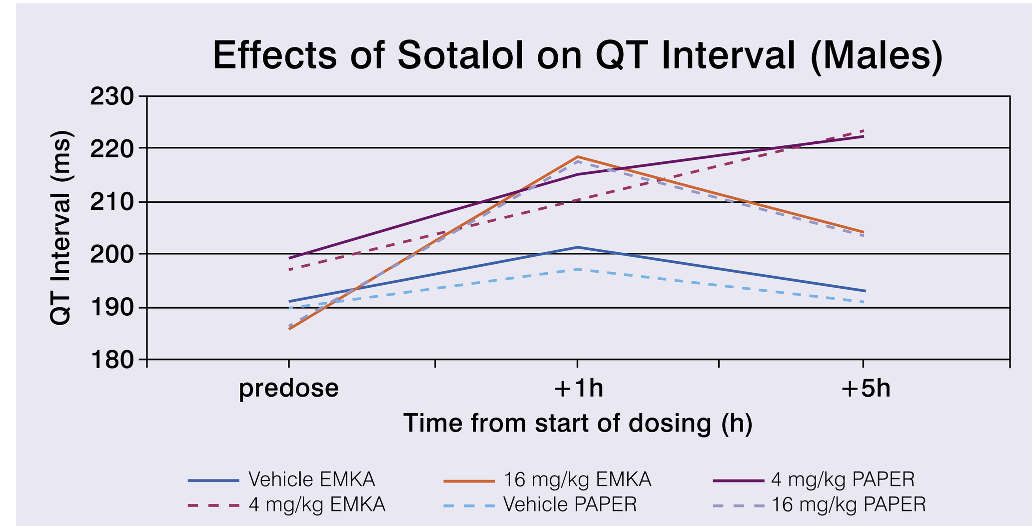

Figure 1

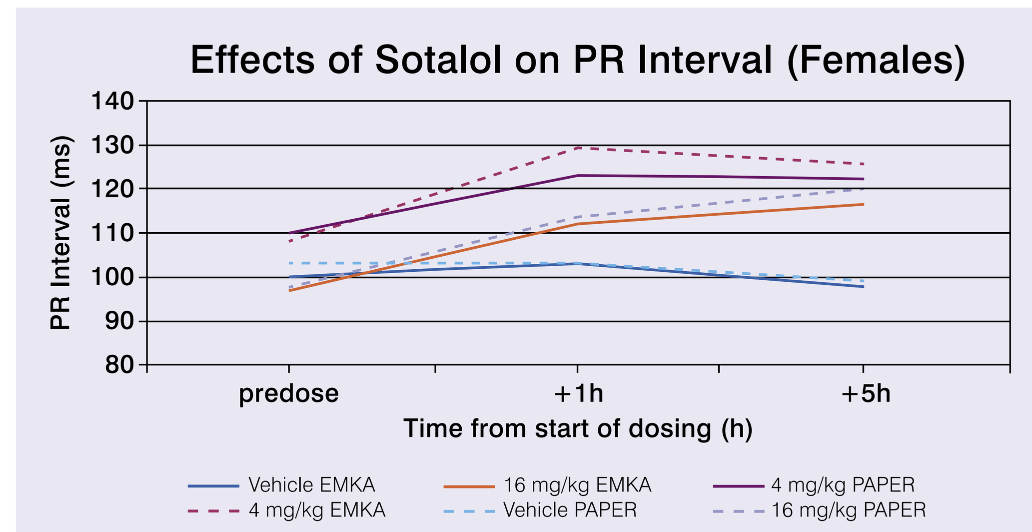

Figure 2

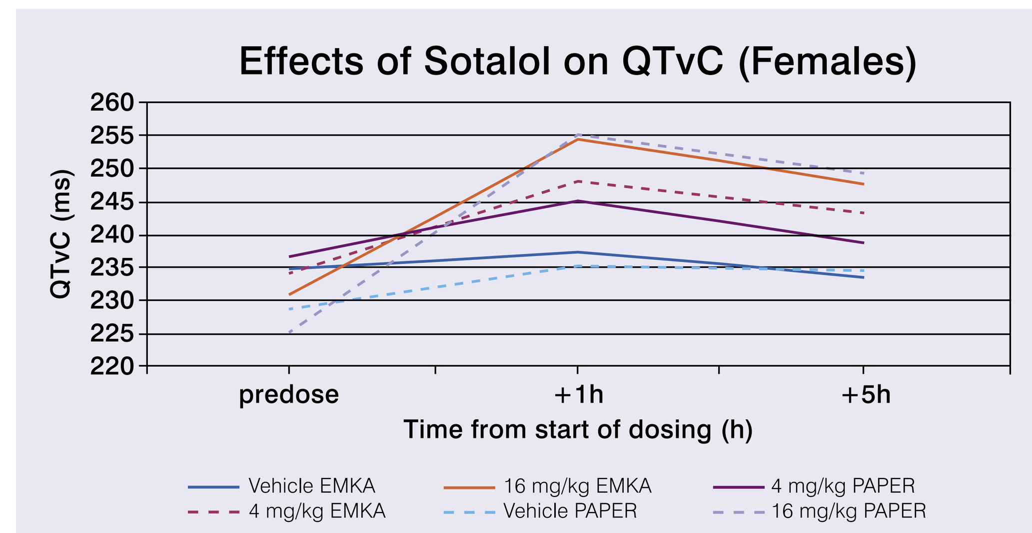

Figure 3

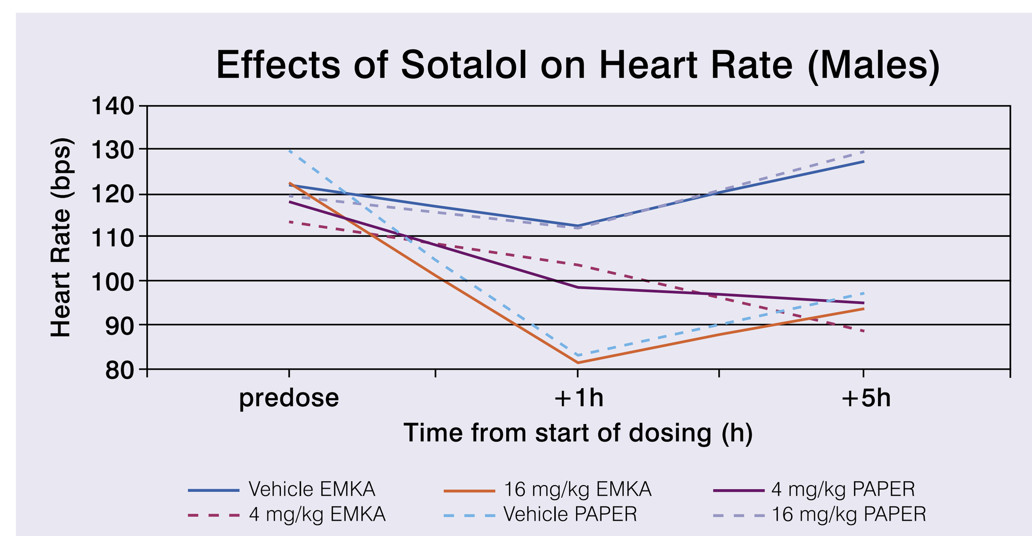

Figure 4

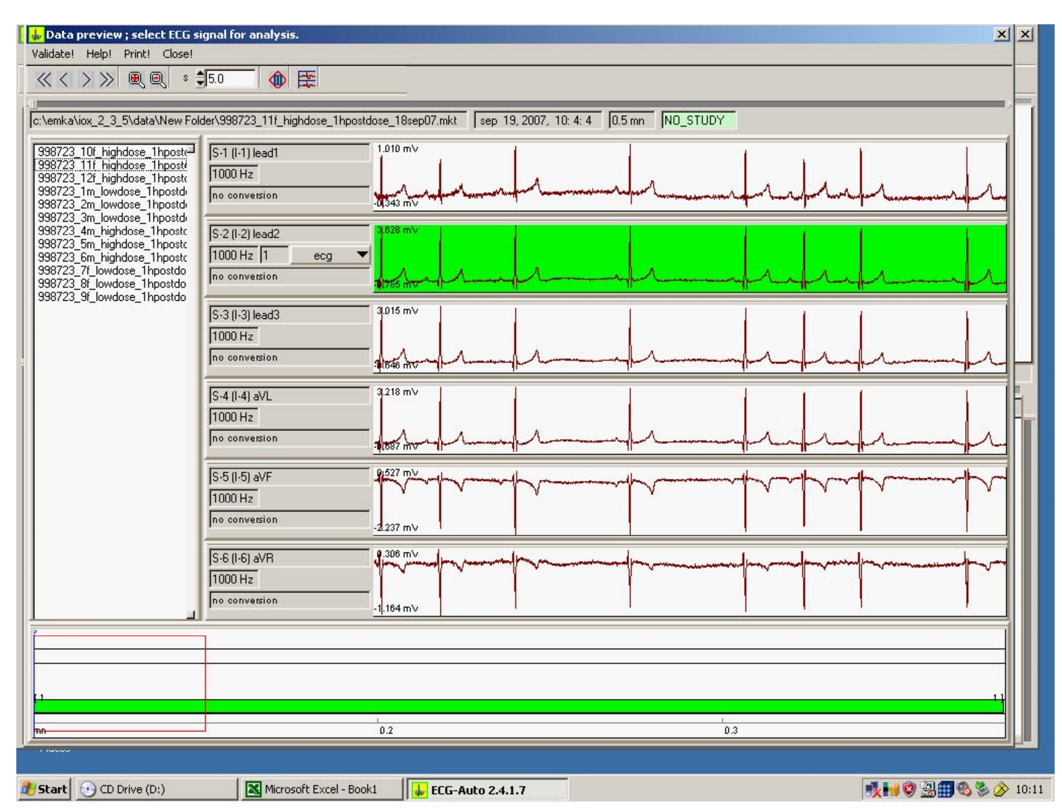

Figure 5. Display of 6 lead ECG

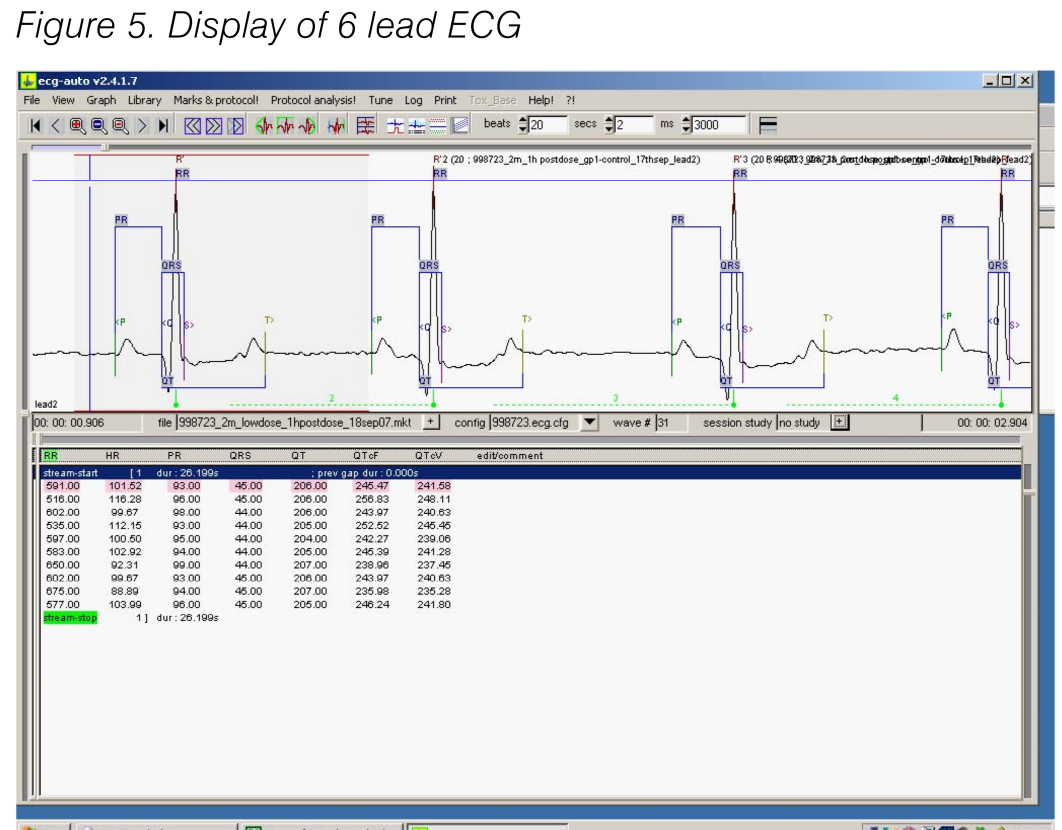

Figure 6. ECG analysis

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