



Aalborg Universitet

AALBORG UNIVERSITY  
DENMARK

## Technical report

*Inter- and intra-rater reliability of regional gastrointestinal transit times measured using the 3D-Transit electromagnet tracking system*

Kalsi, G K; Grønlund, D; Martin, J; Drewes, A M; Scott, S M; Birch, M J

*Published in:*  
Neurogastroenterology and Motility

*DOI (link to publication from Publisher):*  
[10.1111/nmo.13396](https://doi.org/10.1111/nmo.13396)

*Publication date:*  
2018

*Document Version*  
Accepted author manuscript, peer reviewed version

[Link to publication from Aalborg University](#)

*Citation for published version (APA):*

Kalsi, G. K., Grønlund, D., Martin, J., Drewes, A. M., Scott, S. M., & Birch, M. J. (2018). Technical report: Inter- and intra-rater reliability of regional gastrointestinal transit times measured using the 3D-Transit electromagnet tracking system. *Neurogastroenterology and Motility*, 30(11), [e13396]. <https://doi.org/10.1111/nmo.13396>

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

### Take down policy

If you believe that this document breaches copyright please contact us at [vbn@aub.aau.dk](mailto:vbn@aub.aau.dk) providing details, and we will remove access to the work immediately and investigate your claim.

1 **Title**

2 Technical report: Inter- and intra-rater reliability of regional gastrointestinal transit  
3 times measured using the 3D-Transit electromagnet tracking system

4 **Authors and affiliations**

5 G.K. Kalsi<sup>1,2</sup>, D. Grønlund<sup>3,4</sup>, J. Martin<sup>2</sup>, A. M. Drewes<sup>3,4</sup>, S. M. Scott<sup>1</sup>, M. J. Birch<sup>1,2</sup>

6

7 <sup>1</sup>GI Physiology Unit, The Blizard Institute, Barts and the London School of Medicine and Dentistry,  
8 Queen Mary University of London, London, UK

9

10 <sup>2</sup>Clinical Physics, Barts Health NHS Trust, The Royal London Hospital, London, UK

11

12 <sup>3</sup>Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital,  
13 Aalborg, Denmark

14

15 <sup>4</sup>Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

16

17

18

19

19 **Corresponding Author**

20

21 Gursharan Kaur Kalsi

22 Clinical Physics, Barts Health NHS Trust, The Royal London Hospital, 56-76 Ashfield Street,

23 Whitechapel, London. E1 1BB

24 Email: [g.k.kalsi@qmul.ac.uk](mailto:g.k.kalsi@qmul.ac.uk)

25

26

## 27 **Abstract**

28

29 **Background:** The 3D-Transit electromagnet tracking system is an emerging tool for the ambulatory  
30 assessment of gastrointestinal (GI) transit times and motility patterns, based on the anatomical  
31 localization of ingestible electromagnetic capsules. Currently, 3D-Transit recordings are manually  
32 analyzed to extract GI transit times. As this is a subjective method, there is some inherent  
33 variability in the measurements, which may be experience-dependent. We therefore assessed  
34 inter- and intra-rater reliability of GI transit times from 3D-Transit recordings.

35 **Methods:** Thirty-six 3D-Transit recordings (17 female; median age: 34 years (range: 21–80)) were  
36 analyzed twice by 3 raters with varying experience. Each rater manually identified the timestamps  
37 when a capsule progressed from antrum to duodenum, and from ileum to right colon. These  
38 timestamps, along with the ingestion and expulsion times were used to determine whole gut  
39 (WGTT), gastric emptying (GET), small intestinal (SITT) and colonic (CTT) transit times. Reliability  
40 was determined using interclass correlation coefficient (ICC).

41 **Key Results:** For capsule progression timestamps, the most and mid-experienced raters had fair to  
42 good inter- and excellent intra-rater reliability ( $ICC_{\min-\max}=0.61-1.00$ ), whereas the inexperienced  
43 rater had poor to fair inter- and poor intra-rater reliability ( $ICC_{\min-\max}=0.28-0.55$ ). GET and SITT  
44 reliability between the most and mid-experienced raters was fair ( $ICC_{\min-\max}=0.61-0.73$ ), while  
45 reliability between these raters and the inexperienced rater was poor to fair ( $ICC_{\min-\max}=0.28-0.55$ ).  
46 CTT reliability was excellent between and within all raters ( $ICC_{\min-\max}=0.92-0.99$ ).

47 **Conclusions & Inferences:** Inexperienced raters provide the least reliable measurements from 3D-  
48 Transit recordings, which confirms requirement for adequate training. Automation may improve  
49 reliability of measurements.

## 50 **Key Points**

- 51 • The 3D-Transit System can aid the diagnostic evaluation of gastrointestinal disorders. We  
52 assessed the reliability of regional GI transit times measured by experienced and inexperienced  
53 raters.
- 54 • Reliability of gastric emptying and small intestinal transit time was fair between the most and  
55 mid-experienced raters but poor for the inexperienced rater. Whole gut and colonic transit  
56 time reliability was excellent across all raters.
- 57 • Inexperienced raters require adequate training to provide reliable measurements of GI transit  
58 times from the 3D-Transit System.

## 59 **Key Words**

61 3D-Transit system, electromagnetic capsule, gastrointestinal, reliability, transit time

## 62 **Abbreviations**

64 GI: gastrointestinal; cpm: contractions per minute; WGTT: whole gut transit time; GET: gastric  
65 emptying; SITT: small intestinal transit time; CTT: colonic transit time; ICC: intraclass correlation  
66 coefficient; CI: confidence interval.

## 67 **Introduction**

68

69 The 3D-Transit electromagnet tracking system (Motilis Medica, SA, Lausanne, Switzerland) is a novel  
70 and minimally invasive tool for the ambulatory evaluation of total and regional gastrointestinal (GI)  
71 transit times and motility patterns. It accurately tracks and measures the position and orientation  
72 of up to three ingestible electromagnetic capsules from ingestion to expulsion using an external  
73 detector plate positioned over the abdomen.<sup>1-4</sup>

74

75 Total GI transit time is easily extracted from a 3D-Transit recording, as the signal start and end points  
76 indicate capsule ingestion and expulsion times. For regional GI transit times however, the  
77 timestamps when a capsule progresses from the stomach into the duodenum, and from the ileum  
78 into the right colon are manually identified by visually observing changes in the capsule's orientation  
79 angles, which reflect GI contractile activity, along with shifts in its position as it progresses from one  
80 GI region to the next.<sup>1,5</sup>

81

82 The system was originally developed using a stationary detector matrix which required subjects to  
83 stay relatively immobile for long periods of time in a controlled laboratory environment, thus  
84 reducing the effects of external movement artefacts.<sup>6-9</sup> Accordingly, inter-rater variability in capsule  
85 progression timestamps, and thereby GI transit times, has been reported as low.<sup>6,8</sup> The principle  
86 advantage of the ambulatory system is that it enables continuous monitoring of GI motility under  
87 physiological conditions; however, subject ambulation renders it susceptible to external magnetic  
88 fields and motion artifacts, making it more difficult to identify capsule progression timestamps.  
89 Hence, the accuracy in identifying these timestamps is not only dependent on the quality of the

90 recording but also on the ability of the rater to distinguish artifacts from real movements of the  
91 capsule.

92

93 Recently, the inter-variability of GI transit time measurements was assessed by two experienced  
94 raters who analyzed 20 3D-Transit recordings.<sup>1</sup> Differences in regional GI transit times were  
95 reported in 8 of the 20 recordings (40%); however, these differences were considered acceptable  
96 by the authors, as the overall median difference was zero minutes.<sup>1</sup> Nevertheless, there is a need  
97 to determine the level of reliability of measurements, particularly when raters are blinded to their  
98 own and each other's results. Therefore, the primary aim of this study was to assess inter- and intra-  
99 rater reliability of capsule progression timestamps, and hence regional GI transit times. A secondary  
100 aim was to assess how the experience of the rater influences the identification of these timestamps.

101

## 102 **Materials & Methods**

103

### 104 **3D-Transit recording selection**

105 3D-Transit recordings were selected from a database of healthy volunteer studies conducted at the  
106 Neurogastroenterology Unit at Aarhus University Hospital (Aarhus, Denmark), Department of  
107 Gastroenterology and Hepatology at Aalborg University Hospital (Aalborg, Denmark) and the GI  
108 Physiology Unit at Queen Mary University (London, UK) between March 2012 and February 2016.  
109 In these studies, healthy volunteers swallowed up to three capsules, each taken a day apart after an  
110 overnight fast. Recordings were selected if they were complete with clear ingestion and expulsion  
111 points. For studies where volunteers ingested more than one capsule, only one recording was

112 selected irrespective of capsule number. Poor quality recordings or recordings with more than 2  
113 hours of missing data were excluded from the study. From this, a sample of 36 3D-Transit recordings  
114 were randomly selected (17 female; median age: 34 years (range: 21–80)), 12 from each research  
115 center.

116

### 117 **Data Collection**

118 Three independent raters with varying experience of analyzing 3D-Transit recordings participated  
119 in the study. Rater experience was based on the number of previously analyzed recordings as  
120 follows:  $\geq 100$  recordings: most experienced (rater 1); approximately 40 recordings: mid-  
121 experienced (rater 2);  $< 5$  recordings: least experienced (rater 3). All raters were prescribed written  
122 instructions on analyzing 3D-Transit recordings (dated May 2017) and the 3D-Transit System  
123 Instructions for Use (dated September 2014).

124

125 Recordings were analyzed using the 3D-Transit software, version 0.4 (Motilis Medica, SA, Lausanne,  
126 Switzerland). This involved identifying four timestamps as described by Haase et al. (2014)<sup>1</sup>: **(i)**  
127 **ingestion**: start of recording; **(ii) duodenum**: capsule's progression from the stomach into the  
128 duodenum; **(iii) right colon**: capsule's progression from the distal ileum to the caecum; **(iv)**  
129 **expulsion**: end of recording indicated by a loss of signal. For intra-rater reliability, each rater  
130 analyzed the 36 recordings twice with a minimum period of two weeks between repeat analyses.

131

### 132 **Data Analysis**

133 The timestamps were used to determine WGTT (whole gut transit time; time between capsule  
134 ingestion and expulsion), GET (gastric emptying; time between ingestion and passage into the

135 duodenum), SITT (small intestinal transit time; time between the duodenum and right colon  
136 timestamps) and CTT (colonic transit time; time between the right colon timestamp and capsule  
137 expulsion). Transit times were automatically extracted from the 3D-Transit software and exported  
138 as text files for inter- and intra-rater comparison.

139

## 140 **Statistical Analysis**

141 To calculate inter- and intra-rater reliability of the duodenum and right colon timestamps and  
142 regional transit times, the ICCs (intraclass correlation coefficients) and their 95% confidence  
143 intervals (CIs) were calculated based on a single rating, absolute agreement, 2-way random-effects  
144 model. ICC values range between 0 and 1 with a higher value indicating better reliability (<0.5, poor;  
145 0.5-0.75, fair; 0.75-0.9, good; >0.9, excellent).<sup>10</sup> The timestamps were subtracted from the ingestion  
146 timestamp to convert the data into hours for the ICCs to be determined. Scatterplots, means and  
147 95% CI were used to illustrate and compare GI transit times within and between raters. All statistical  
148 analyses were performed using SPSS Statistics Version 25 (IBM, New York, USA).

149

## 150 **Results**

151

### 152 **Inter-rater reliability of duodenum and right colon timestamps**

153 Between raters, the degree of inter-rater reliability of both the duodenum and right colon  
154 timestamps was poor, with the ICC ranging between 0.42 and 0.47 (95% CI = 0.24-0.63). However,  
155 when comparing the most and mid-experienced raters, the reliability of both timestamps was fair  
156 to good. Reliability between raters 1 (most-experienced) and 2 (mid-experienced) against rater 3



157 (least-experienced) was poor to fair for the duodenum timestamp and very poor for the right colon  
158 timestamp (Table 1).

159

#### 160 **Intra-rater reliability of duodenum and right colon timestamps**

161 Intra-rater reliability of both timestamps was good to excellent for raters 1 and 2 with the ICC  
162 ranging between 0.89 and 1.00 (95% CI = 0.79-1.00). However, reliability of these timestamps was  
163 poor for rater 3 (Table 1).

164

#### 165 **Inter-rater reliability of regional GI transit times**

166 Scatterplots for inter-rater reliability of whole gut and regional GI transit times are presented in  
167 Figure 1. GET and SITT reliability between all raters was low, supported by poor ICCs ranging  
168 between 0.41 and 0.47 (95% CI = 0.25-0.63), while reliability of CTT was excellent (Table 2). ICC  
169 values for GET and SITT were consistently fair between raters 1 and 2, while reliability between  
170 these raters and rater 3 was poor. WGTT reliability was excellent across all raters.

171

#### 172 **Intra-rater reliability of regional GI transit times**

173 Scatterplots for intra-rater reliability are presented in Figure 2. For raters 1 and 2, good to excellent  
174 intra-rater reliability was seen for GET and SITT, with ICC values ranging between 0.84 and 1.00 (95%  
175 CI = 0.71-1.00), while reliability was poor for rater 3 (ICC = 0.20-0.48, 95% CI = -0.14-0.71) (Table 2).  
176 CTT and WGTT reliability was excellent for all raters.

177

178 **Discussion**

179

180 We assessed the inter- and intra-rater reliability of regional GI transit times based on the manual  
181 identification of the duodenum and right colon capsule progression timestamps in 3D-Transit  
182 recordings. Our results showed that the inter- and intra-rater reliability of both timestamps is  
183 generally fair to excellent amongst the most and mid-experienced raters and as expected, poor in  
184 an inexperienced rater. This explains the fair inter-rater, and good to excellent intra-rater reliability  
185 of GET and SITT seen amongst the more and mid experienced raters. However, reliability of these  
186 transit times was poor in the inexperienced rater, indicating a need for an adequate period of  
187 training.

188

189 Surprisingly, the inter- and intra-rater reliability of CTT was excellent amongst all raters. This was  
190 unexpected, as the CTT is dependent on the right colon timestamp, the reliability of which was poor  
191 in the inexperienced rater. Furthermore, general consensus amongst all raters was that the right  
192 colon timestamp was subjectively more difficult to identify than the duodenum. However, this may  
193 be explained by examining the magnitudes of the measurements. CTT is approximately eight times  
194 longer than GET, and four times longer than SITT; therefore, the CTT measurement is less sensitive  
195 to the uncertainty in the right colon timestamp due to its large magnitude and a fixed capsule  
196 expulsion timestamp.

197

198 Nevertheless, it is apparent that the manual method of analyzing 3D-Transit recordings is not  
199 optimal, even amongst experienced raters who only showed fair inter-rater reliability for GET and  
200 SITT. Furthermore, the reliability of GI transit times was assessed using good quality recordings.

201 Poorer quality recordings, which are difficult to interpret due to the increased presence of artifacts  
202 may produce less reliable measurements. Therefore, there is a need to improve the current  
203 methodology to obtain better estimates of GI transit times. This may be achieved through  
204 automation by using artifact rejection algorithms and pattern-recognition techniques to better  
205 detect the various gut contraction frequencies and hence, the capsule progression timestamps.

206

207 In conclusion, we assessed the inter- and intra-rater reliability of GI transit times as measured using  
208 the 3D-Transit system. Reliability was generally fair between experienced raters. An inexperienced  
209 rater provided the least reliable results, indicating a need for adequate training. Automation may  
210 improve reliability of the method.

211

## 212 **Acknowledgements**

213 We acknowledge the assistance of Dr. Jonathan Reeves for the selection of the 3D-Transit  
214 recordings.

215

## 216 **Funding**

217 Researchers were indirectly funded from their research and training positions.

218

219

## 220 **Disclosure**

221

222 The authors have no competing interests.

223

224

225

226

227 **Author Contribution**

228

229

230 GKK and MJB designed the study. GKK, DG and JM collected the data. GKK and DG analyzed the

231 data and drafted the initial manuscript. GKK completed and finalized the manuscript. AMD, SMS

232 and MJB reviewed and approved the final manuscript as submitted. All authors have approved this

233 version of the manuscript.

234

235

236 **References**

- 237 1. Haase AM, Gregersen T, Schlageter V, et al. Pilot study trialling a new ambulatory method  
238 for the clinical assessment of regional gastrointestinal transit using multiple  
239 electromagnetic capsules. *Neurogastroenterol Motil.* 2014;26(12):1783-1791.  
240
- 241 2. Haase AM, Gregersen T, Christensen LA, et al. Regional gastrointestinal transit times in  
242 severe ulcerative colitis. *Neurogastroenterol Motil.* 2016;28(2):217-224.  
243
- 244 3. Poulsen JL, Nilsson M, Brock C, Sandberg TH, Krogh K, Drewes AM. The Impact of Opioid  
245 Treatment on Regional Gastrointestinal Transit. *Journal of neurogastroenterology and*  
246 *motility.* 2016;22(2):282-291.  
247
- 248 4. Mark EB, Poulsen JL, Haase AM, et al. Assessment of colorectal length using the  
249 electromagnetic capsule tracking system: a comparative validation study in healthy  
250 subjects. *Colorectal disease : the official journal of the Association of Coloproctology of*  
251 *Great Britain and Ireland.* 2017;19(9):O350-o357.  
252
- 253 5. Gronlund D, Poulsen JL, Sandberg TH, et al. Established and emerging methods for  
254 assessment of small and large intestinal motility. *Neurogastroenterol Motil.* 2017;29(7).  
255
- 256 6. Stathopoulos E, Schlageter V, Meyrat B, Ribaupierre Y, Kucera P. Magnetic pill tracking: a  
257 novel non-invasive tool for investigation of human digestive motility. *Neurogastroenterol*  
258 *Motil.* 2005;17(1):148-154.  
259
- 260 7. Hiroz P, Schlageter V, Givel JC, Kucera P. Colonic movements in healthy subjects as  
261 monitored by a Magnet Tracking System. *Neurogastroenterol Motil.* 2009;21(8):838-e857.  
262
- 263 8. Worsoe J, Fynne L, Gregersen T, et al. Gastric transit and small intestinal transit time and  
264 motility assessed by a magnet tracking system. *BMC Gastroenterol.* 2011;11:145.  
265
- 266 9. Hedsund C, Joensson IM, Gregersen T, Fynne L, Schlageter V, Krogh K. Magnet tracking  
267 allows assessment of regional gastrointestinal transit times in children. *Clin Exp*  
268 *Gastroenterol.* 2013;6:201-208.  
269
- 270 10. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for  
271 Reliability Research. *J Chiropr Med.* 2016;15(2):155-163.  
272

273 **Figure Legends**

274 Figure 1: Inter-rater reliability of total and regional GI transit times compared across raters where  
275 rater 1 is most experienced, rater 2 is mid-experienced and rater 3 is least experienced. GET, gastric  
276 emptying; SITT, small intestine transit time; CTT, colonic transit time; WGTT, whole gut transit time.  
277 All transit times are in hours.

278

279 Figure 2: Comparison of first and repeat analyses to assess intra-rater reliability of total and regional  
280 GI transit times within raters, where rater 1 is most experienced, rater 2 is mid-experienced and  
281 rater 3 is least experienced. GET, gastric emptying; SITT, small intestine transit time; CTT, colonic  
282 transit time; WGTT, whole gut transit time. All transit times are in hours.

283

284 **Table Captions**

285 Table 1: Inter- and intra-rater reliability of duodenum and right colon timestamps between and  
286 within raters of varying levels of experience where rater 1 (R1) is most experienced, rater 2 (R2) is  
287 mid-experienced and rater 3 (R3) is least experienced.

288

289

290 Table 2: Inter- and intra-rater reliability of regional GI transit times between and within raters of  
291 varying levels of experience where rater 1 (R1) is most experienced, rater 2 (R2) is mid-experienced  
292 and rater 3 (R3) is least experienced. GET, gastric emptying; SITT, small intestine transit time; CTT,  
293 colonic transit time; WGTT, whole gut transit time.

294

295 **Table 1**

TEST	ICC (95% CI)
<b>INTER-OBSERVER ANALYSIS</b>	
<b>Duodenum Timestamp</b>	
R1-R2-R3 <sup>''</sup>	0.47 (0.32 – 0.63)
R1-R2 <sup>†</sup>	0.61 (0.45 – 0.75)
R1-R3 <sup>†</sup>	0.55 (0.38 – 0.71)
R2-R3 <sup>†</sup>	0.47 (0.27 – 0.65)
<b>Right Colon Timestamp</b>	
R1-R2-R3 <sup>''</sup>	0.42 (0.24 – 0.60)
R1-R2 <sup>†</sup>	0.82 (0.72 – 0.89)
R1-R3 <sup>†</sup>	0.28 (0.10 – 0.48)
R2-R3 <sup>†</sup>	0.30 (0.11 – 0.50)
<b>INTRA-OBSERVER ANALYSIS</b>	
<b>Duodenum Timestamp</b>	
R1 <sup>§</sup>	0.96 (0.92 – 0.98)
R2 <sup>§</sup>	1.00 (0.99 – 1.00)
R3 <sup>§</sup>	0.48 (0.16 – 0.71)
<b>Right Colon Timestamp</b>	
R1 <sup>§</sup>	0.89 (0.79 – 0.94)
R2 <sup>§</sup>	0.93 (0.87 – 0.96)
R3 <sup>§</sup>	0.28 (-0.34 – 0.55)

''Pooled values from 6 measurements (first and repeat analyses)

† Pooled values from 4 measurements (first and repeat analyses)

§Pooled values from 2 measurements (first and repeat analyses)

296

297

298

299

300

301

302

303

304

305

306

307

308

309

310

311 **Table 2**

TEST	MEAN (95% CI)*	ICC (95% CI)
<b>INTER-RATER ANALYSIS</b>		
<b>Gastric Emptying Time (GET)</b>		
R1-R2-R3 <sup>''</sup>	3.2 (2.8-3.6)	0.47 (0.32-0.63)
R1-R2 <sup>†</sup>	3.7 (3.1-4.2)	0.61 (0.45-0.75)
R1-R3 <sup>†</sup>	2.6 (2.3-2.9)	0.55 (0.38-0.71)
R2-R3 <sup>†</sup>	3.3 (2.8-3.8)	0.47 (0.27-0.65)
<b>Small intestine transit time (SITT)</b>		
R1-R2-R3 <sup>''</sup>	6.3 (5.8-6.8)	0.41 (0.25-0.58)
R1-R2 <sup>†</sup>	7.3 (6.7-8.0)	0.73 (0.61-0.84)
R1-R3 <sup>†</sup>	6.1 (5.5-6.7)	0.28 (0.11-0.48)
R2-R3 <sup>†</sup>	5.6 (5.1-6.1)	0.32 (0.15-0.51)
<b>Colonic transit time (CTT)</b>		
R1-R2-R3 <sup>''</sup>	24.3 (22.4-26.2)	0.94 (0.88-0.97)
R1-R2 <sup>†</sup>	22.8 (20.5-25.2)	0.98 (0.97-0.99)
R1-R3 <sup>†</sup>	25.2 (22.8-27.5)	0.93 (0.84-0.97)
R2-R3 <sup>†</sup>	25.0 (22.6-27.3)	0.92 (0.82-0.96)
<b>INTRA-RATER ANALYSIS</b>		
<b>Gastric Emptying Time (GET)</b>		
R1 <sup>§</sup>	3.0 (2.5-3.4)	0.96 (0.92-0.98)
R2 <sup>§</sup>	4.4 (3.4-5.4)	1.00 (0.99-1.00)
R3 <sup>§</sup>	2.2 (1.9-2.5)	0.48 (0.16-0.71)
<b>Small intestine transit time (SITT)</b>		
R1 <sup>§</sup>	7.9 (6.9-8.9)	0.86 (0.75-0.93)
R2 <sup>§</sup>	6.8 (6.0-7.6)	0.84 (0.71-0.92)
R3 <sup>§</sup>	4.4 (3.8-4.9)	0.20 (-0.14-0.50)
<b>Colonic transit time (CTT)</b>		
R1 <sup>§</sup>	23.0 (19.7-26.3)	0.99 (0.98-0.99)
R2 <sup>§</sup>	22.7 (19.3-26.0)	0.99 (0.98-1.00)
R3 <sup>§</sup>	27.3 (24.0-30.6)	0.97 (0.94-0.99)

\* Values expressed in hours

<sup>''</sup>Pooled values from 6 measurements (first and repeat analyses)

<sup>†</sup> Pooled values from 4 measurements (first and repeat analyses)

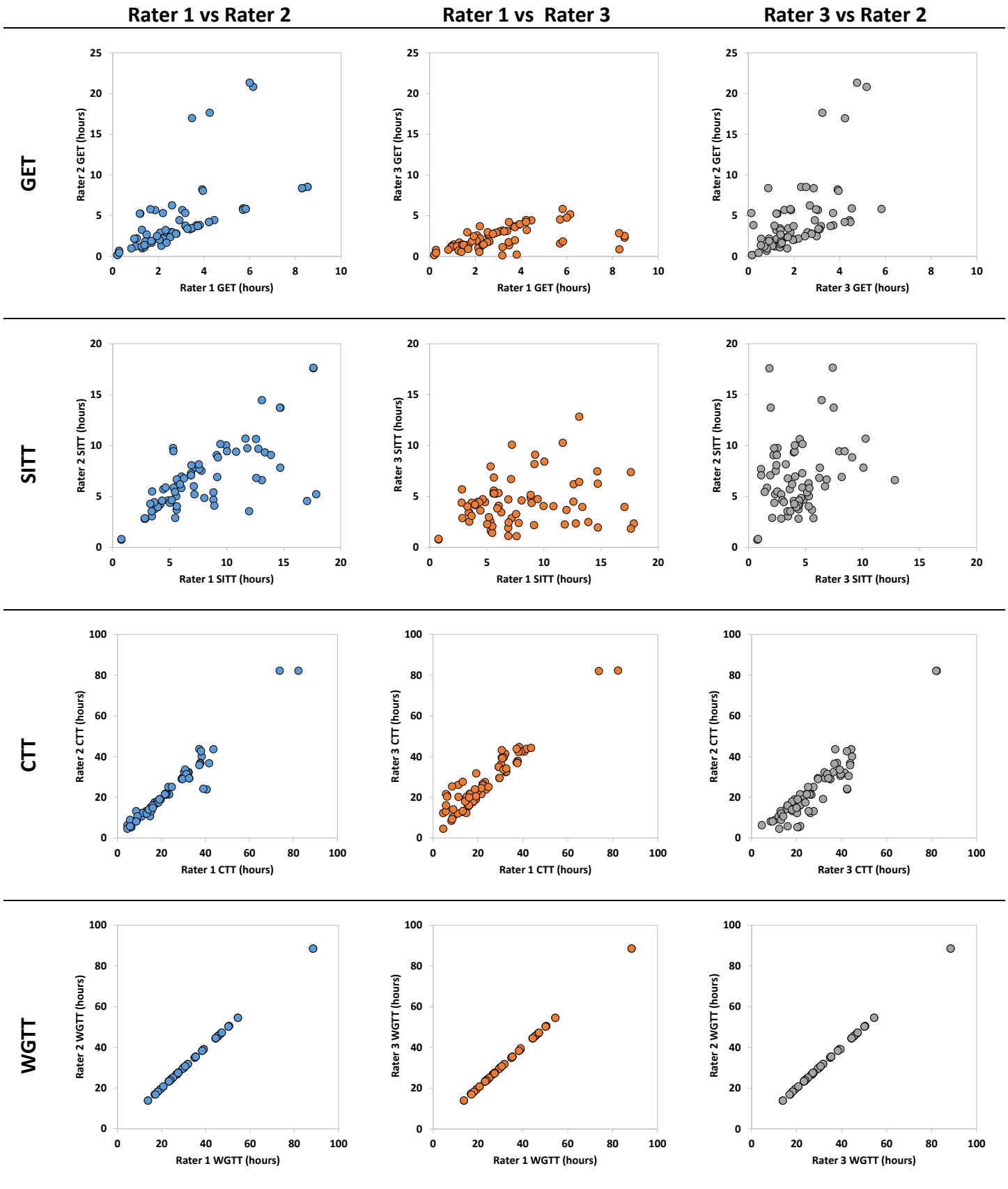
<sup>§</sup>Pooled values from 2 measurements (first and repeat analyses)

312

313



314 **Figure 1**



315 **Figure 2**

