Published in final edited form as:

J Biomech. 2016 November 07; 49(15): 3741–3745. doi:10.1016/j.jbiomech.2016.09.044.

Characterizing Fluoroscopy Based Kinematic Accuracy as a Function of Pulse Width and Velocity

Arin M. Ellingson, Ph.D.^{1,2,5}, Joseph D. Mozingo^{2,3}, Dixon J. Magnuson⁴, Mark W. Pagnano, M.D.¹, and Kristin D. Zhao, Ph.D.²

¹Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN, USA

²Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, MN, USA

³Biomedical Engineering and Physiology Graduate Program, Mayo Clinic, Rochester, MN, USA

⁴Department of Radiology, Mayo Clinic, Rochester, MN, USA

⁵Department of Physical Medicine and Rehabilitation, University of Minnesota, Minneapolis, MN, USA

Abstract

Fluoroscopic imaging has become increasingly popular to investigate total knee arthroplasty kinematics non-invasively - 3D implant models are aligned with 2D image projections, and optimized via an edge-contour alignment technique. Previous studies have quantified the accuracy of this approach, however they do not adequately address the impact of image collection parameters. A particularly sensitive parameter is the pulse width, or exposure time per frame. At longer pulse widths, a more motion is captured in a single frame; this can lead to image blur and subsequent degradation to image edge quality. Therefore, the comparative accuracy of relative joint kinematics as a function of pulse width and joint velocity needs to be defined. A limits of agreement approach was taken to define the mean differences between optoelectric kinematic measures (gold standard) and fluoroscopic methods at various pulse widths (1, 8, 16ms) and knee velocities (50, 100, 225°/s). The mean absolute differences between the optoelectric and fluoroscopic methods for 1ms pulse width was less than 1.5° and 0.9mm. Comparable rotational differences (1.3°) were observed for the 8ms pulse width but had larger translational differences (1.4mm). The 16ms pulse width yielded the greatest mean differences (2.0° and 1.6mm), which increased with knee flexion velocity. The importance of pulse width and velocity should not be overlooked for future studies - this parameter has proven to be a sensitive metric in the quantification of joint motion via fluoroscopy and must be identified and reported in future studies.

*Corresponding Author: Kristin D. Zhao, Ph.D., Rehabilitation Medicine Research Center, Assistive and Restorative Technologies Laboratory, Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, MN 55905, zhao.kristin@mayo.edu.

Conflicts of Interest Statement

The authors have no conflicts of interest to report related to this research study.

Keywords

Knee; Joint Kinematics; Fluoroscopy; Accuracy; Agreement; Pulse Width; Arthroplasty; Knee Replacement

Introduction

Fluoroscopic imaging has become an increasingly popular method to investigate total knee arthroplasty (TKA) kinematics non-invasively using shape-matching techniques. Briefly, the position and orientation of a 3D implant models are aligned with 2D image projections of its x-ray, and optimized via an edge-contour alignment algorithm (Figure 1) (Mahfouz et al. 2003). Prior studies aimed to assess the accuracy of this shape-matching technique have reported absolute accuracies on the order of a millimeter and sub-degrees (Banks and Hodge 1996; Mahfouz et al. 2003; Yamazaki et al. 2004). Relative joint kinematics has reported errors of less than 2.1 degrees and 1.9 mm using a single plane fluoroscopy system (Acker et al. 2011; Lebel et al. 2011). It is important to note that many of these studies determine accuracy based on a foam model of the bones without soft tissue – an idealistic case without added noise from surrounding musculature and skin. Internal validation experiments are a critical step prior to clinical research. However, many recent studies do not perform their own validation, but rely on previously published accuracy measurements, which likely may not reflect the accuracy of their own system and process (Fujimoto et al. 2016; Nakamura et al. 2015; Okamoto et al. 2014). Furthermore, inexperienced fluoroscopy research teams may utilize available clinical units, for which parameters are often difficult to customize. The lack of customizability may result in lengthened or automatic exposure times not controlled or reported by the researcher. Therefore, without proper knowledge of one's own equipment and attention to detail, inadequate data can be collected and thus improper conclusions potentially made. Another critical component often lacking in recently published work are the study's fluoroscopic imaging parameters, which likely have a significant effect on kinematic accuracy.

A particularly sensitive parameter in dynamic imaging with fluoroscopy is the pulse width, or exposure time per frame. In an effort to reduce radiation to as low as reasonably achievable (ALARA) levels, many fluoroscopy systems use a pulsed sequence, rather than continuous exposure with no shutter. The length of the pulse width is simply analogous to the exposure time per frame, and is directly related to the amount of motion that can occur within the frame. At longer pulse widths, a greater amount of motion is captured in a single frame at a given object's velocity; this can lead to image blur and subsequent degradation to image edge quality – a critical factor for the shape-matching technique. The importance of this phenomenon has been nicely, yet anecdotally described previously (Tashman 2008). However, to our knowledge, no studies have quantified the errors associated with increased pulse widths and movement velocity. *Therefore, the purpose of this study was to assess the accuracy of 6 degree-of-freedom relative TKA kinematics as pulse width and flexion velocity were systematically varied.*

Methods

With the approval from our institutional biospecimens committee, one intact, fresh-frozen male (91 yrs.) cadaver right leg was acquired from the Mayo Clinic Bequest Program. Appropriately sized femoral (size 5) and tibial (size 4) total knee replacement components (Triathlon® Knee System, Stryker Orthopaedics, Mahwah, NJ, USA) were implanted by an orthopedic surgeon using a standard surgical approach. To facilitate digitization, small slits in the skin on the medial and lateral aspects of the femur and tibia were created to expose landmarks used to establish local anatomical coordinate systems (Grood and Suntay 1983).

The proximal femur and distal tibia were potted in bone cement and secured upright in a custom apparatus that allowed for unconstrained knee flexion (30° to 80°), which mimicked passive rotation of the knee immediately post-operation at a manually guided rate. Figure 2 illustrates the apparatus and setup. The linear slide attached to the proximal end of the femur translates vertically and the ankle brace distally allows plantar and dorsiflexion of the foot permitting rotation of the knee joint. The knee was centered in the imaging volume created by the 30×38 cm flat-panel Multi-Diagnost Eleva C-arm single-plane fluoroscopy system (Philips Medical Systems, Best, Netherlands) perpendicular to the primary plane of bending (sagittal plane with a source to image-receptor distance of 1250 mm). Images were collected at a resolution of 512×512 pixels (0.746 mm/pixel). X-ray images were acquired at 30 Hz (63 kV, 160 mA) with varying pulse widths - 1ms, 8ms, and 16ms.

Active infrared marker sets were attached to bone pins that were embedded in the femur and tibia (Ilharreborde et al. 2010). 3D kinematics were simultaneously acquired using an Optotrak Certus at 100 Hz (Northern Digital Inc., Waterloo, Ontario, Canada) and subsequently downsampled to 30 Hz using a custom Matlab script (Matlab®, MathWorks, Natick, MA, USA). The optoelectric system has reported accuracy on the order of 0.2° and 0.15 mm (Baltali et al. 2008; Ilharreborde et al. 2010). The flexion rotation data was used to align the two systems temporally through a point set registration technique utilizing a least squares regression to minimize the differences in the datasets – visual inspection of each dataset confirmed synchronous frames of initial motion for each system. Using a metronome, the knee rotation velocity was varied between 50°/s, 100°/s, and 225°/s in a randomized fashion for each pulse width investigated, which resulted in approximately 120 frames, 60 frames, and 20 frames, respectively since the collection frequency was set at 30 Hz. The ranges of velocities were chosen to be similar to activities of daily living, where the average and peak velocities for a sit-to-stand task is about 50°/s and 100°/s, respectively. Walking rotational velocity on average is approximately 150°/s, while peaks can reach upwards to 350°/s (Kenton R. Kaufman, Ph.D., Personal Communication, February 23, 2015).

Prior to shape-matching, the tibial and femoral implant's CAD file orientation was adjusted to align with the local anatomical coordinate system using a combination of Matlab and Blender (blender.org). Similar to Acker et al., landmarks on the implant were used to create the digital and the anatomical coordinate system (i.e. identifiable landmarks on the implant both digitally (Blender) and physically (Optotrak) were used to create the coordinate systems) (Acker et al. 2011). An open source model-based tracking program was used to

manipulate the position and orientation of 3D CAD models of the femoral and tibial components, such that model edges were coincident with edges of the projected silhouettes on each radiograph frame, Figure 1 (JointTrack, www.sourceforge.net/projects/jointtrack). Following manual placement, poses were optimized with a built-in simulated annealing algorithm and each model's 3D transformation matrix was outputted (Mahfouz et al., 2003). Relative orientation was defined using Euler angles (Z-X-Y sequence; flexion/extension, abduction/adduction, external/internal rotation) based on custom Matlab scripts. This process has shown to be reliable and good intra-class agreement (ICC: 0.94–0.96) (Shi et al. 2014).

The 3D position and orientation of the tibia relative to the femur were determined for all frames of each trial and the “limits of agreement” were defined using a Bland-Altman technique (Acker et al. 2011; Bland and Altman 1999). This method compares the differences between the two collection techniques relative to their mean, and allows the 95% limits of agreement to be quantified.

Results

The average absolute kinematic differences between the optoelectric and fluoroscopic methods for the shortest, 1 ms, pulse width investigated were 1.5° and 0.9 mm or less with 95% limits of agreement spanning less than 2.9° and 3.5 mm for all flexion velocities (Table 1). Figure 3 depicts the Bland-Altman plots demonstrating the agreement between the two kinematic collection techniques for all translations and rotations at 1 ms pulse width for knee velocities of 50°/s, approximately the average flexion velocity for a sit-to-stand activity. Bland-Altman plots for the maximum velocity at 1 ms are displayed in Figure 4. A linear trend was detected only in the abduction rotation ($R^2=0.73$). The overall largest differences were in abduction-adduction across trials, but varied in translation. Comparable mean absolute differences in rotation were observed for the 8 ms pulse width – less than 1.3°. However, translations increased to 1.4 mm (Table 1). The 16 ms pulse width yielded the greatest mean differences, which were intensified during the greatest knee flexion velocity. The mean rotational and translational absolute differences increased to 2.0° and 1.6 mm, respectively. Furthermore, the 95% limits of agreement between the systems also increased considerably for the 16ms pulse width with a maximum of 7.7° and 5 mm. Figure 5 highlights the effect increasing the pulse width and flexion velocity on the in-plane rotation (Flexion/Extension).

Discussion

This study aimed to determine the relative kinematic accuracy of a fluoroscopic shape-matching technique based on pulse width and knee flexion velocity. As expected, the minimal pulse width allowed on the fluoroscopy system with the lowest velocity– 1 ms pulse width; 50°/s – yielded the smallest differences between the collection methods. The mean absolute differences were 0.4, 0.7, and 0.7° for flexion, abduction, and internal rotation, respectively and 0.5, 0.3, and 0.7 mm for anterior, superior, and lateral, respectively (Figure 3; Table 1). The differences between the systems, as well as the limits of agreement, increased with rates of flexion velocity. Even at the highest flexion velocity, the 1 ms pulse

width produced results well within acceptable limits where a maximum mean absolute difference of 1.5° and 0.9 mm were measured.

Similar differences and limits of agreement were observed for trials completed at an 8 ms pulse width, with the exception of medial/lateral translations during the maximal flexion velocities, where the limits of agreement increased 3 fold from the 1 ms pulse width. The in-and-out of plane translations are notoriously the most error prone because of projection errors. This error is exacerbated with increased blur since the tracked object potentially appears larger, due to more motion on each frame (Figure 5B, C). The largest pulse width (16 ms) generated the largest differences, especially for the faster activities, yielding the largest mean absolute differences observed. The limits of agreement were also larger, even for the primary plane of bending, flexion-extension. Figure 5 summarizes the changes associated with increasing the pulse width and flexion velocity, where the mean differences and limits of agreement are very similar for all pulse widths at low velocity (50°/s) but increase dramatically at higher velocity (225°/s).

The mean differences and limits of agreement reported herein for the 1 and 8 ms pulse widths for all flexion velocities were within previously reported values that were upwards to 2.1° and 1.9mm (Acker et al. 2011). Additionally, these errors are much less than those experienced using traditional skin-markers (Miranda et al. 2013), demonstrating the utility of fluoroscopic based kinematic assessment. Yet, as evaluation of boney motion via pulsed fluoroscopy gains in popularity, it is critical for researchers to define, report, and optimize their systems since the pulse width and speed of activity have an effect on the accuracy of the system. They should not and cannot assume their system and workflow will produce accuracy levels equivalent to previous published work.

The purpose of this study was to investigate the relationship between pulse width and velocity on the kinematic errors associated with shape-matching. The results must be contextualized within the scope of the limitations of the study, which include the application to only one joint. Although the principle can be extrapolated to other joints, proper validation of each system needs to be performed. This includes for each joint and motion of interest – as the accuracy values are likely to be affected. Also, only one specimen was included in the analysis. However, this did produce hundreds of dynamic frames, which were independently compared against the optoelectric frame, providing a sufficient sample size for the analysis performed. Additionally, even though great care was taken to identify the anatomical landmarks to be digitized and used for creating the local coordinate system, differences in coordinate systems between the optoelectric and fluoroscopic is an area prone to error. An external motion analysis system was chosen over a roentgen stereophotogrammetric analysis (RSA) approach because RSA is also impacted by the imaging parameters, since it also relies on fluoroscopic acquisition. Despite this, the relative limits of agreement identified between the 3 pulse widths (1, 8, and 16 ms) should remain valid since the coordinate systems do not change from trial to trial. This may be responsible for the linear trend observed in abduction-adduction, or more likely because as the knee undergoes flexion, valgus ensues, which causes rotation in and out of the imaging plane. Similar trends were reported previously (Acker et al. 2011). The maximal flexion velocity that was investigated was limited due to the manually guided nature of the apparatus, and

therefore velocities of peak walking or running could not be collected. It is hypothesized the greater the rotational and linear velocity, the larger the error experienced and this would be exacerbated with longer pulse widths.

In conclusion, this work defines the accuracy of our fluoroscopy system in conjunction with a 2D/3D shape-matching protocol for TKA models. This provides a basis for future trials investigating TKA kinematics *in vivo*. Internal validation studies are an essential first step prior to initiating clinical research. Additionally, the importance of pulse width and velocity should not be overlooked for future studies – larger pulse widths should be used cautiously and pulse widths of 16ms and greater avoided. This parameter has proven to be a sensitive metric in the quantification of joint motion via fluoroscopy and must be identified and reported in future studies.

Acknowledgments

Funding was provided through NIH/NIAMS T32AR56950 and Minnesota Partnership for Biotechnology and Medical Genomics. The authors thank Stryker Orthopedics for providing the instrumentation, devices, and CAD files for the implants. The company had no contribution in study design and results.

References

- Acker, Stacey, et al. Accuracy of Single-Plane Fluoroscopy in Determining Relative Position and Orientation of Total Knee Replacement Components. *Journal of Biomechanics*. 2011; 44(4):784–87. [PubMed: 21092967]
- Baltali, Evre, et al. Accuracy and Precision of a Method to Study Kinematics of the Temporomandibular Joint: Combination of Motion Data and CT Imaging. *Journal of Biomechanics*. 2008; 41(11):2581–84. [PubMed: 18617178]
- Banks, Scott A.; Hodge, W Andrew. Accurate Measurement of Three-Dimensional Knee Replacement Kinematics Using Single-Plane Fluoroscopy. *IEEE Transactions on Biomedical Engineering*. 1996; 43(6):638–49. <http://www.ncbi.nlm.nih.gov/pubmed/8987268>. [PubMed: 8987268]
- Bland JM, Altman DG. Measuring Agreement in Method Comparison Studies. *Statistical Methods in Medical Research*. 1999; 8(2):135–60. <Go to ISI>://WOS:000083700100004. [PubMed: 10501650]
- Fujimoto, Eisaku, et al. Intra-Operative Gaps Affect Outcome and Postoperative Kinematics in Vivo Following Cruciate-Retaining Total Knee Arthroplasty. *International Orthopaedics*. 2016; 40(1):41–49. [PubMed: 26133289]
- Grood ES, Suntay WJ. A Joint Coordinate System for the Clinical Description of Three-Dimensional Motions: Application to the Knee. *J Biomech Eng*. 1983; 105(2):136–44. <http://www.ncbi.nlm.nih.gov/pubmed/6865355>. [PubMed: 6865355]
- Ilharreborde B, et al. A Dynamic Method for in Vitro Multisegment Spine Testing. *Orthop Traumatol Surg Res*. 2010; 96(4):456–61. <http://www.ncbi.nlm.nih.gov/pubmed/20452304>. [PubMed: 20452304]
- Lebel BP, et al. Total Knee Arthroplasty Three-Dimensional Kinematic Estimation Prevision. From a Two-Dimensional Fluoroscopy Acquired Dynamic Model. *Orthopaedics & Traumatology: Surgery & Research*. 2011; 97(2):111–20.
- Mahfouz MR, Hoff WA, Komistek RD, Dennis DA. A Robust Method for Registration of Three-Dimensional Knee Implant Models to Two-Dimensional Fluoroscopy Images. *IEEE Trans Med Imaging*. 2003; 22(12):1561–74. <http://www.ncbi.nlm.nih.gov/pubmed/14649746>. [PubMed: 14649746]
- Miranda DL, Rainbow MJ, Crisco JJ, Fleming BC. Kinematic Differences between Optical Motion Capture and Biplanar Videoradiography during a Jump-Cut Maneuver. *J Biomech*. 2013; 46(3): 567–73. <http://www.ncbi.nlm.nih.gov/pubmed/23084785>. [PubMed: 23084785]

- Nakamura, Shinichiro, et al. Analysis of the Flexion Gap on In Vivo Knee Kinematics Using Fluoroscopy. *Journal of Arthroplasty*. 2015; 30(7):1237–42. <http://dx.doi.org/10.1016/j.arth.2015.01.046>. [PubMed: 25680453]
- Okamoto, Nobukazu, et al. In Vivo Kinematic Comparison between Mobile-Bearing and Fixed-Bearing Total Knee Arthroplasty during Step-up Activity. *Journal of Arthroplasty*. 2014; 29(12): 2393–96. <http://dx.doi.org/10.1016/j.arth.2014.02.022>. [PubMed: 24698817]
- Shi, Xiaojun, et al. In Vivo Kinematics Comparison of Fixed- and Mobile-Bearing Total Knee Arthroplasty during Deep Knee Bending Motion. *Knee Surgery, Sports Traumatology, Arthroscopy*. 2014; 22(7):1612–18.
- Tashman, Scott. Comments on ‘Validation of a Non-Invasive Fluoroscopic Imaging Technique for the Measurement of Dynamic Knee Joint Motion’. *J Biomech*. 2008; 41(15):3290–93. <http://www.ncbi.nlm.nih.gov/pubmed/18930460>. [PubMed: 18930460]
- Yamazaki T, et al. Improvement of Depth Position in 2-D/3-D Registration of Knee Implants Using Single-Plane Fluoroscopy. *IEEE Trans Med Imaging*. 2004; 23(5):602–12. <http://www.ncbi.nlm.nih.gov/pubmed/15147013>. [PubMed: 15147013]

Figure 1. Workflow of 2D/3D Shape Matching

Left: 3D TKA models aligned with silhouette when knee is initially fully extended (A) and fully flexed (B). **Middle:** Silhouette of 1ms pulse width at initial position (C) and position of maximal flexion velocity (D). **Right:** Silhouette of 16ms pulse width at initial position (E) and at maximal flexion velocity (F).

Figure 2. Collection set-up depicting custom apparatus allowing unconstrained knee flexion-extension

The linear slide attached to the proximal end of the femur translates vertically and the ankle brace distally allows plantar and dorsiflexion of the foot permitting rotation of the knee joint. The fluoroscopy system is positioned perpendicular to the primary plane of bending (sagittal plane for flexion-extension). Active Optotrak marker sets are rigidly attached to the femur and tibia for simultaneous kinematic collection with the fluoroscope. *Foam bone model is shown only for display purposes – study was performed on cadaveric lower extremity with all surrounding soft tissue and intact ankle joint.*

Figure 3. Bland-Altman plots (Pulse Width: 1ms/Flexion Velocity: 50°/s)

Demonstrate agreement in kinematic measures between fluoroscopic and optoelectronic methods for 1ms pulse width, 50°/s rotation rate trial. Each point represents the mean and difference of relative joint angles (top row) and translations (bottom row) between each method, at a given frame. The dashed and solid lines are the mean difference between methods, and the 95% confidence intervals respectively.

Figure 4. Bland-Altman plots (Pulse Width: 1ms/Flexion Velocity: 225°/s

Demonstrate agreement in kinematic measures between fluoroscopic and optoelectronic methods for 1ms pulse width, 225°/s rotation rate trial. Each point represents the mean and difference of relative joint angles (top row) and translations (bottom row) between each method, at a given frame. The dashed and solid lines are the mean difference between methods, and the 95% confidence intervals respectively.

Figure 5. Effect of Pulse Width and Rotational Velocity on Limits of Agreement

A. Box plot showing the mean difference (dashed) and 95% limits of agreement (box) between fluoroscopy and optoelectric kinematics (Flexion/Extension). Mean difference and limits of agreement were similar for all pulse widths at low velocity. At higher velocity the limits of agreement decrease for long pulse widths. **B.** Representative fluoroscopy image of 1 ms pulse width during the 225°/s activity. **C.** Representative fluoroscopy image of 16 ms pulse width during the 225°/s activity; note the blurred edges.

Table 1

Mean differences (bold) and mean absolute differences (bold in brackets) between methods. The 95% limits of agreement in parentheses.

Difference	1ms Pulse Width			8ms Pulse Width			16ms Pulse Width			225 °/s		
	50 °/s	100 °/s	225 °/s	50 °/s	100 °/s	225 °/s	50 °/s	100 °/s	225 °/s	50 °/s	100 °/s	225 °/s
Flexion (deg)	-0.1 [0.4] (-1.4 to 1.3)	1.0 [1.0] (-0.4 to 2.5)	-0.4 [0.9] (-2.7 to 1.9)	0.5 [0.7] (-0.9 to 1.9)	0.5 [0.8] (-1.1 to 2.1)	0.5 [1.0] (-1.8 to 2.8)	-0.2 [0.6] (-1.7 to 1.3)	0.7 [1.1] (-1.7 to 3.1)	0.8 [1.7] (-3.1 to 4.6)			
Abduction (deg)	-0.5 [0.7] (-1.9 to 0.8)	-0.4 [0.6] (-1.7 to 1.0)	-1.2 [1.5] (-3.9 to 1.5)	-1.0 [1.0] (-2.3 to 0.3)	-1.2 [0.9] (-2.8 to 0.5)	-1.2 [1.3] (-3.2 to 0.8)	-0.9 [0.9] (-2.2 to 0.5)	-1.5 [1.5] (-3.1 to 0.1)	-2.0 [2.0] (-4.2 to 0.3)			
Internal (deg)	-0.4 [0.7] (-1.9 to 1.0)	-0.1 [0.6] (-1.7 to 1.4)	-0.4 [0.9] (-2.5 to 1.8)	-0.1 [0.3] (-0.9 to 0.7)	0.2 [0.5] (-1.1 to 1.4)	0.7 [0.8] (-0.7 to 2.0)	0.3 [0.6] (-1.1 to 1.7)	0.2 [0.6] (-1.1 to 1.5)	1.0 [1.1] (-1.0 to 3.0)			
Ant/Post. (mm)	-0.5 [0.5] (-1.5 to 0.6)	-0.4 [0.5] (-1.6 to 0.8)	-0.3 [0.6] (-1.6 to 1.0)	0.3 [0.5] (-0.8 to 1.3)	0.1 [0.4] (-0.9 to 1.0)	0.1 [0.8] (-1.7 to 1.9)	0.1 [0.6] (-1.3 to 1.5)	1.5 [1.5] (0.2 to 2.8)	1.6 [1.7] (-0.9 to 4.0)			
Sup/Inf (mm)	-0.2 [0.3] (-0.9 to 0.6)	0.2 [0.5] (-0.9 to 1.4)	-0.2 [0.5] (-1.7 to 1.2)	-0.4 [0.6] (-1.7 to 0.8)	-0.1 [0.5] (-1.4 to 1.2)	-0.3 [0.8] (-1.9 to 1.4)	-0.3 [0.6] (-1.5 to 0.8)	0.8 [0.9] (-0.5 to 2.2)	-0.9 [1.1] (-2.8 to 1.1)			
Med/Lat (mm)	0.0 [0.7] (-1.8 to 1.7)	-0.2 [0.9] (-2.6 to 2.2)	-0.6 [0.7] (-2.0 to 0.8)	-0.6 [1.0] (-2.7 to 1.4)	0.6 [1.0] (-1.3 to 2.5)	0.8 [1.4] (-2.2 to 3.9)	0.1 [0.9] (-2.1 to 2.2)	-0.6 [1.0] (-3.1 to 1.9)	-0.3 [0.8] (-2.4 to 1.8)			