ORIGINAL ARTICLE



Comparison of standard automotive industry injury predictors and actual injury sustained during significant whiplash events

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Abstract

Purpose We present a unique opportunity to compare standard neck injury criteria (used by the automotive industry to predict injury) with real-life injuries. The injuries sustained during, and the overall kinematics of, a television demonstration of whiplash mechanics were used to inform and validate a vertebral level model of neck mechanics to examine the relevance of current injury criteria used by the automotive industry.

Methods Frontal and rear impact pulses, obtained from videos of sled motion, were used to drive a MADYMO human model to generate detailed segmental level biomechanics. The maximum amplitude of the frontal and rear crash pulses was 166 ms⁻² and 196 ms⁻², respectively, both with a duration of 0.137 s. The MADYMO model was used to predict standard automotive neck injury criteria as well as detailed mechanics of each cervical segment.

Results Whilst the subject suffered significant upper neck injuries, these were not predicted by conventional upper neck injury criteria (Nij and Nkm). However, the model did predict anterior accelerations of C1 and C2 of 40 g, which is 5 times higher than the threshold of the acceleration for alar ligament injury. Similarly, excessive anterior shear displacement (15 mm) of the skull relative to C2 was predicted. Predictions of NIC, an injury criterion relevant to the lower neck, as well as maximum flexion angles for the lower cervical segments (C3–T1) exceeded injury thresholds.

Conclusion The criteria used by the automotive industry as standard surrogates for upper neck injury (Nij and Nkm) did not predict the significant cranio-cervical junction injury observed clinically.

Keywords Human study · Whiplash injury · Neck kinematics · Alar ligaments injury · Madymo

Introduction

Whiplash injury was firstly described by Crowe in 1928 and defined by Downs [1] as "trauma to supporting structures of the neck resulting from forcible forward or backward acceleration of the head with recoil in the opposite direction". Although whiplash injury is not life threatening, it can cause significant long-term pain and disability [2]. Such residual disability occurs in 4.5% of patients and costs the UK economy £3.64 billion [3] and the EU economy 10 billion euros per year [4].

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Most of the cases of whiplash injury occur at low vehicle speed (below 23 kmh⁻¹ (6.4 ms⁻¹)) in "dense traffic situations" [5], when a car with an "unaware victim" is suddenly impacted from the back [6]. Although frontal collisions also cause whiplash motion and account for more than 27% of all whiplash injury reports [7], they are rarely discussed in the literature. Analysis of the descriptions of the whiplash injury mechanism provided by a few authors [3, 5, 8, 9] gives the following sequence of kinematic events in the spine during the whiplash motion caused by a rear-end collision:

- (1) The torso of a car occupant is pushed forward (relative to the position of the head) by the car seat, a phenomenon referred to as "head lag". This motion causes straightening of thoracic kyphotic curve of a car occupant.
- (2) Meanwhile, the neck moves in a whiplash-like manner (S-shaped curvature of the neck is developed) due to the influence of shear force. The following stage



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involves the extension of the neck and the development of a C-shaped curvature.

(3) The extension of the neck is followed by the rebound of the head from a head restraint and subsequent hyperflexion.

Injury criteria are used extensively within the automotive industry (as a surrogate for actual injuries) when designing safety systems (such as restraints and airbags) and for regulatory safety testing. These criteria are mathematical formulations based on the mechanism of injury and measurements of acceleration, force and displacement made using either crash test dummies or computational modelling. It is important to understand that such injury criteria are not the same as actual injuries. Likewise, the validity of these criteria depends greatly on how well their component measurements and calculations correspond to the circumstances of an injury. A large number of injury criteria have been proposed for whiplash neck injuries; this study aims to identify those that are most relevant.

Boström [10] developed the Neck Injury Criterion (NIC), for low-speed rear-end impacts, which is based on the relative horizontal motion between the head and chest. It has an injury threshold of $15 \text{ m}^2\text{s}^{-2}$ and is calculated by:

$$NIC = a_{rel} * 0.2 + v_{rel}^2$$
 (1)

where $a_{\rm rel}$ and $v_{\rm rel}$ are relative horizontal acceleration and velocity between T1 and C1. NIC has been validated against tests using cadavers [11], dummies [12] and human volunteers [13].

Many studies [9, 14–16], have proposed that the influence of the abnormal forces and bending moments caused by the motion of a neck beyond the normal physiological limits during the whiplash motion causes stretching of the facet joins of the ligaments leading to their rupture. Eppinger [17] developed the Normalized Neck Injury Criterion (N_{ij}) relevant to the neck injuries in frontal impacts based upon combining measurements of axial force and flexion/extension moment normalized by dividing by the relevant failure conditions. This is calculated according to the following equation:

$$N_{ij} = F_Z/F_{\text{int}} + M_Y/M_{\text{int}} \tag{2}$$

where F_Z is the axial load, M_Y is the flexion/extension bending moment. $F_{\rm int}$ and $M_{\rm int}$ represent critical intercept values used for normalization.

Similar to N_{ij} , the Neck Protection Criterion ($N_{\rm km}$) was proposed by Schmitt [18] for rear impacts. $N_{\rm km}$ uses a combination of anterior/posterior shear force and flexion/extension bending moment. It is calculated by:



where F_X is the shear force, M_Y is the flexion/extension bending moment. F_{int} and M_{int} represent critical intercept values used for normalization.

Based on the hypothesis that the rotation of two adjacent vertebrae beyond the physiological limit may lead to the neck soft tissue injury, Panjabi [19] proposed the Intervertebral Neck Injury Criterion (IV–NIC). It is a simple normalization of segmental flexion by the physiological range of motion at that level:

$$IV - NIC = \theta_{\text{dynamic}}(t) / \theta_{\text{physiological}}$$
 (4)

where $\theta_{\rm dynamic}$ is the intervertebral rotation, $\theta_{\rm physiological}$ is the physiological range of motion (ROM), t-represents time.

There is a particular issue for validating injury criteria relating to whiplash injuries; the primary validation for such criteria is normally comparison with cadaveric studies. However, these studies, whilst excellent at recording bone fractures, are not good at identifying minor soft tissue lesions. A number of clinical studies have demonstrated that ligaments are damaged more seriously than bony structures during the whiplash motion, and that these soft tissue injuries are often relatively minor. For example, Saternus [20] found that among 397 patients with whiplash-associated disorders 85.6% had injuries of ligaments and only 14.4%—bone injuries. Similarly, the motion of the neck during in the impact phase is influenced strongly by the level of neck muscle contraction [21] which is difficult to simulate in cadaveric tests.

Among the most vulnerable ligamentous structures of the craniovertebral junction are the alar ligaments [22] –two symmetrical strong, "cord-like" structures that extend laterally from the posterior surface of the dens of C2 (Axis) to the occipital condyles of the skull [23]. Vulnerability of the alar ligaments is caused by their high stiffness with mostly collagen and a little elastic composition [24] which means that high stresses are developed for small deformations. This may lead to tearing of the ligaments even in small deformations, such as a whiplash motion [25]. Although the tears of the alar ligaments may lead to serious disorders and even death [20, 22], the dynamic behaviour of these ligaments during the whiplash motion still remains unknown.

Only a few attempts to evaluate injury mechanisms of the alar ligaments during whiplash motion have been observed. Maak [25] described a temporal pattern of the alar ligaments strain and demonstrated peaks of the ligaments' elongation in the conditions of different accelerations using a mechanical model of the whole cervical spine. However, none of the previous studies demonstrated the sequence of kinematic events in the C0–C2 segment which could cause strains and ruptures of the alar ligaments during the whiplash motion.



As neck motion data are not collected during real-world automotive collisions, much research has therefore been conducted using volunteer studies. However, to prevent serious injury, the impact magnitudes are deliberately kept small and by definition neck injuries comparable to those seen in automotive impacts are not generated [26, 27].

In this study we are able to take advantage of a situation where whiplash impacts causing significant neck injury were captured using high speed video. Two archive high speed video recordings of a poorly specified demonstration for a television documentary that led to the serious injury of the presenter were analysed. These videos were recorded as part of a science TV programme aiming to attract attention of a target audience to the consequences of car crashes for children sitting in forward-facing and rear-facing car seats. It should be noted that the authors of this paper had no part in the design and staging of this demonstration and that the videos became available for study at a later date. These videos show the movement of the spine and head of a 42-year-old male volunteer (weight 76 kg, height 181 cm) sitting on a sled at the moment of the frontal and rear-end impacts. The videos were recorded at 1000 frames per second. The velocity of the sled before the collisions was 7 ms⁻¹ (25 kmh⁻¹). One video of the frontal collision and one of the rear-end collision were analysed.

The aim of this study was to evaluate the relevance of a number of standard injury criteria to real-life injuries sustained by the documentary presenter. The motion of the sled and the neck kinematics of the subject were used to set the boundary conditions and provide basic validation of a kinematic model of the subject, respectively. The model was then used to predict the values and directions of C0–C2 and C7 vertebral acceleration, shear forces acting on the cervical vertebrae, C0–C2 vertebral displacements, NIC, IV–NIC, Nij and Nkm. The injury criteria predications were then compared to the actual injuries sustained by the subject so that their relevance could be established.

Methods

Clinical assessment

The subject was assessed clinically by one of the authors (LM) one year after the collisions. This assessment was performed before the biomechanical analysis and was therefore blind to its results. A lateral flexion stress test [28], was preformed to evaluate the integrity of the alar ligaments in a supine and neutral position only (due to subject comfort). Similarly, the Sharp-Purser test to assess the integrity of the transverse ligaments could not be performed as it was deemed to be contraindicated, the subject being unable to safely and comfortably perform the required movements.

Measurement from the high speed video

Frames were taken at every 1 ms of the original video. The control lines and dots were manually determined on each

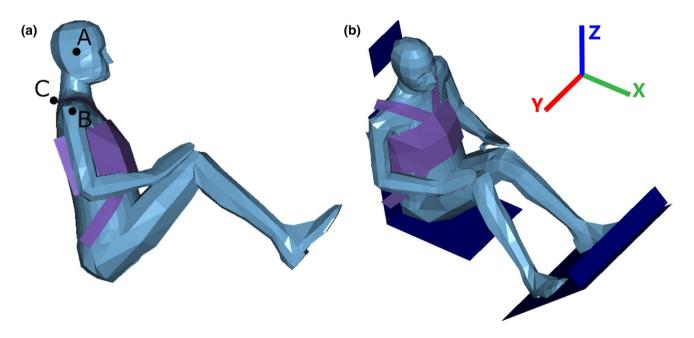


Fig. 1 50th percentile man facet model with the determined control lines and dots (a) and with the developed seat and belts (b) during the simulations in MADYMO



frame using ImageJ software (NIH and LOCI, University of Wisconsin). They are demonstrated on MADYMO human model in Fig. 1a.

- A—current position of the head (left auditory canal) and B—current position of the shoulder (left acromium)—for measurement of the displacement of the head and shoulder;
- (2) C—current position of the sled (upper point of a belt attachment to the sled)—for measurement of a sled displacement.

The displacement data of the head, shoulder and sled were filtered with a CFC10 filter before velocities were calculated, no filtering was applied to the calculated velocities and a CFC60 filter was applied to the calculated accelerations. The sled accelerations (calculated from displacement values) were used for the sled acceleration pulses used to drive the MADYMO model described below.

Model description

We used the industry standard automotive kinematic software MADYMO (TASS International) for the modelling because it is the software currently used by the majority of automotive manufacturers for the development of their safety systems. It is therefore the neck injury criteria that are predicted by this software that are used to minimize neck injury in whiplash type impacts.

The model used in the simulation of the motion of the participant was a 50th percentile man facet model in MADYMO (version 6.1). This model has been extensively validated for various loading conditions against a number of human and post mortem human surrogate tests. Two major categories of tests were used for validation: volunteer tests for low severity loading and post-mortem human surrogate tests for higher severity loading. The first group of tests included blunt impacts with different impact locations (head, shoulder, thorax, abdomen, pelvis and legs). These tests used different impact specifications ranging from 1.83 to 9.9 m/s. The second was conducted on the cadaveric model sitting on sled on both rigid and car seats using different directions of the impacts (frontal, rear, lateral, vertical and rollover). The acceleration pulse specifications in these tests ranged from 1 to 15 g. A further group of tests included vertical and frontal vibration tests with a frequency specifications of 0.35-15 Hz [29].

The anthropometry of the 50th percentile man facet model is very similar to the dimensions of the volunteer of the whiplash injury study (height 1.76 m, weight 75.3 kg vs. height 1.81 m weight 76 kg). Finite element models of a sled and three belts were developed and added to the human model to complete the physical configuration. The

sled consisted of the head restraint, footrest, seat cushion and seat back. A system of 3 belts (one horizontal and two crossing in front of the chest) was used to simulate the restraint used by the subject. The human model was seated on the sled in an initial posture matching that of the whiplash injury study participant: with the spine straight, legs bent, head held straight and the hands resting on the thighs (Fig. 1b). The feet of the model was placed into a stable position on the footrest (with the toes pointing out).

Analysis procedure

Figure 2 shows the crash pulses for the frontal and rear-end collisions obtained from the analysis of the videos. These crash pulses were applied to the MADYMO model in the direction of the X-axis. Additionally, the acceleration of gravity (9.81 ms⁻²) was applied to the human model in the direction of the Z-axis.

The following settings of the MADYMO solver were used during the simulations: run time -1 s; time step 1.0×10^{-5} s; integration method used for the multi-body equations of motion – Explicit-implicit Euler integration method with fixed time step; dynamic analysis type, which results in determining the time history response of the model. The following model output signals were recorded: body outputs (velocity of C0–T1, acceleration of C0–T1, angular positions of C0–T1, relative position of C0–C2) and joint constraint outputs (C0–C7 force and torque).

NIC, IV-NIC, Nij and Nkm were computed in order to predict the risk of sustaining injuries of the upper and lower neck structures. Values of the cervical vertebral accelerations and shear forces acting on the C0-C7 vertebrae were measured. The flexion/extension angle of each cervical segment was calculated from the relative rotation of adjacent vertebrae. In order to determine if the upper cervical vertebrae underwent displacements that might be potentially damaging for the alar ligaments, which are located at the cranio-vertebral junction, the relative displacements between C0 and C2 were measured.

Further model validation

The motion of the MADYMO human model was validated qualitatively against the motion captured from the video. Displacements of the head and shoulder of the study participant relative to the headrest and of the MADYMO human model were compared. The shoulder and head displacements of the model corresponded well to the motion of the participant during the impact phase (up to 160 ms) with peak displacements in agreement to better than 5 mm in all cases (Figs. 3, 4). However, the correspondence



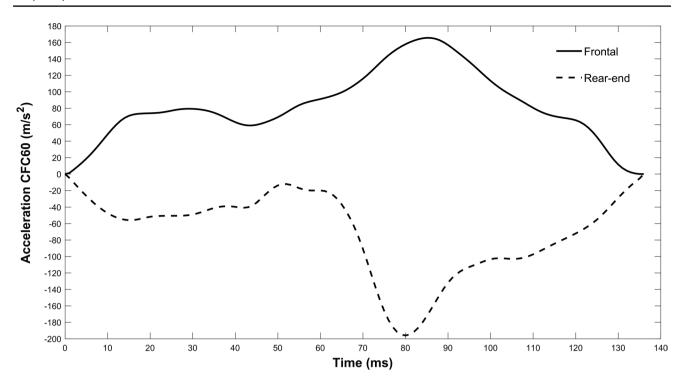


Fig. 2 Crash pulses applied to the MADYMO human model during the simulation of the frontal and rear-end collisions

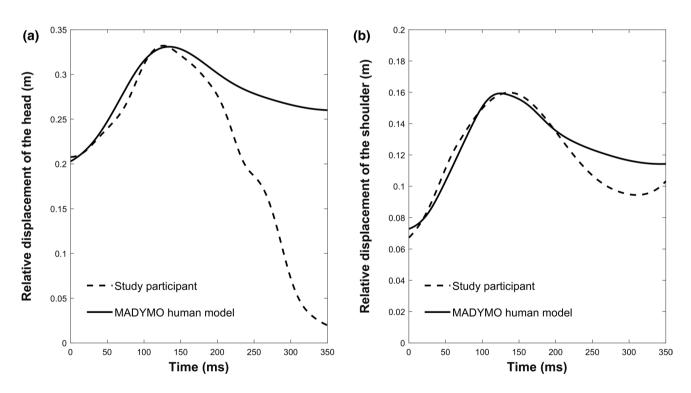


Fig. 3 Displacement of the head and shoulder relative to the headrest in the direction of the X axis during the frontal collision of the whiplash injury study participant and the human model in MADYMO



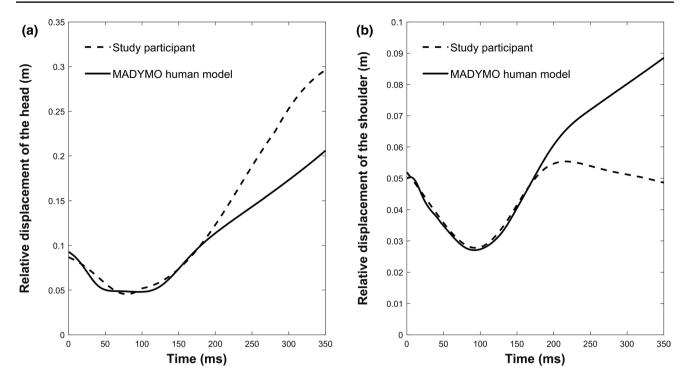


Fig. 4 Displacement of the head and shoulder relative to the headrest in the direction of the X axis during the rear-end collision of the whiplash injury study participant and the human model in MADYMO

during the rebound phase was less good, possibly due to the active motion of the participant. For this reason, we limit our analysis to the period of 0–160 ms where correspondence is good.

Results

Clinical findings

Given a severe restriction in range of motion, the test for alar ligament integrity was difficult to perform and to interpret, however abnormalities in both the quality and a range of movement at the occipito-atlanto-axial complex were palpated. Further assessment of the subject suggested that there was severe disruption to the transverse ligament, as well as some laxity in the alar ligaments, thereby creating a state of instability in the cranio-cervical junction.

There were further palpatory findings in the cervical spine including an anterior shear of C6 and C7 relative T1, coupled with significant involvement of the posterior and anterior structures of the cervical spine including the dural membranes, nuchal ligament, and extensive muscular guarding, especially in the suboccipital region.

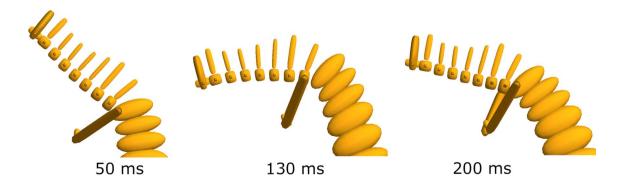


Fig. 5 Neck geometry at key points in the frontal collision



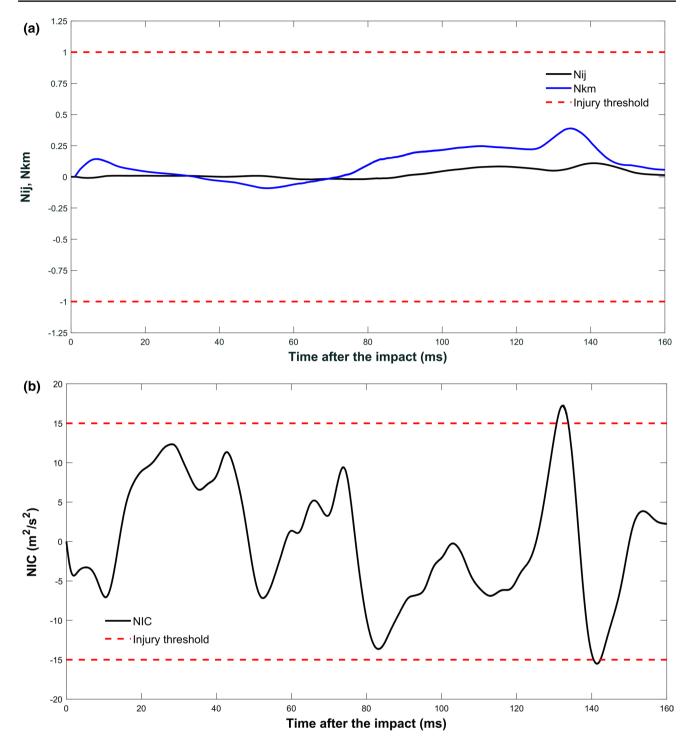


Fig. 6 Neck injury criteria, Nij and Nkm (a), NIC (b) and IV-NIC (c) during the simulation of the frontal collision

Frontal collision

For the frontal collision the motion of the head and neck can be divided in the following phases: (1) 0–120 ms—forward motion of the head; (2) 110–150 ms—maximum protraction of the head, hyperflexion of the neck and the chin's contact

with a chest; (3) 150–200 ms—rearward motion of the head (Fig. 5).

Figure 6 shows the values of the standard neck injury criteria. Injuries were not predicted by Nij and Nkm but were predicted by NIC and IV–NIC. Neither Nij nor Nkm came close to exceeding the injury threshold. The peak



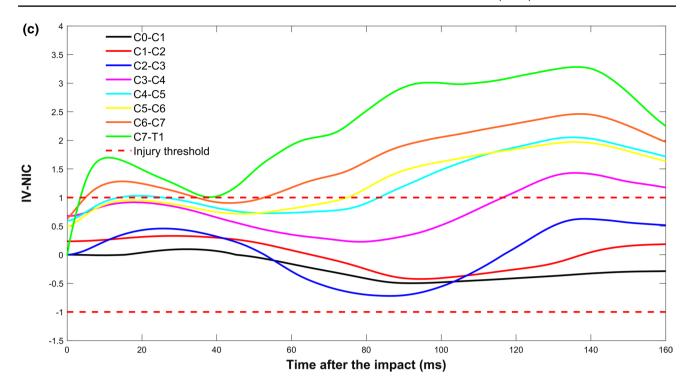


Fig. 6 (continued)

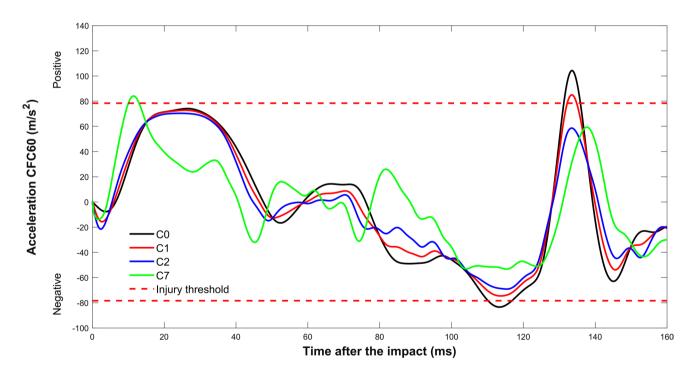


Fig. 7 Vertebrae' accelerations in the direction of the X-axis during the simulation of the frontal collision

value of NIC (a function of relative anterio-posterior motion of the head and chest) was 17.2 m²s⁻² exceeding the injury threshold at the moment of maximum head protraction (130 ms). At the same point of time, IV–NIC

(a function of segmental flexion/extension relative to the physiological range of motion), exceeded the injury threshold for all levels below C3.



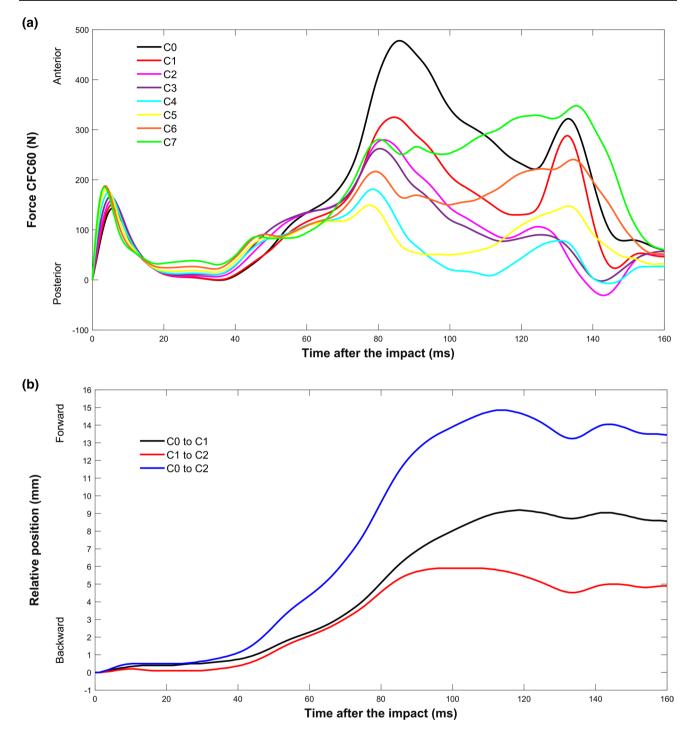


Fig. 8 Antero-posterior forces (a) acting on the vertebrae of the cervical spine and the resulting displacements (b) in the simulation of the frontal collision

Figure 7 shows the anterio-posterior acceleration of C0–C2 and C7 vertebrae as a function of time. The threshold for alar ligament injury was exceeded, again, at the maximum protraction of the neck.

The backward translation of the trunk relative to the head during the frontal impact produced shear force in the lower cervical vertebrae (Fig. 8a). The peak anterior force occurred at C0 (478 N) during the head's forward motion



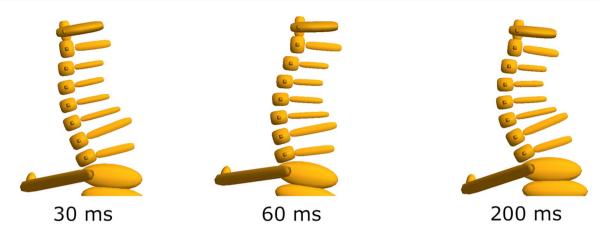


Fig. 9 Neck geometry at key points in the rear collision

(85 ms). The displacement of C0 relative to C2 reached its maximum value (15 mm) at 115 ms (Fig. 8b).

Rear-end collision

For the rear-end collision the motion of the head and neck can be divided in the following phases: 1) 0–50 ms – extension of the neck; 2) 50–140 ms – collision of the head with a headrest; 3) 140–250 ms – the rebound of the head from a head restraint and forward motion of the head (Fig. 9).

Figure 10 shows the injury criteria throughout the collision. Injury is predicted by NIC and IV–NIC (at the C6-T1 level only), whilst Nij and Nkm do not predict injury. The maximum value of NIC (80 m²s⁻²) was achieved when the head impacted the headrest (Fig. 10b). Figure 10c shows that the IV–NIC exceeds its injury threshold of 1 at the C6–T1 levels, reaching the peak value of 1.48.

Figure 11 shows the antero-posterior accelerations C0–C2 and C7 as a function of time. The C0–C2 vertebrae were subjected to approximately 35–40 g acceleration (alar ligaments injury threshold=8 g) lasting for a very short time (10 ms) during the head's contact with a headrest.

Figure 12 shows the anteroposterior shear force acting on the cervical vertebrae and the resulting shear displacement. During the head's contact with the headrest (50–140 ms), shear forces acting on all cervical vertebrae quickly change from posterior to anterior, with the highest load occurring at C0 (246 N). The rearward motion of the head and contact with the headrest (50–140 ms) caused a backward translation of C0 relative to C1 and C1 relative to C2. During the head's forward motion (140–200 ms) backward translation of C0 relative to C2 reached its highest value (9.2 mm).

Discussion

The crash pulse used for this television documentary was inappropriate for in vivo human volunteer testing. As a result, significant signs and symptoms were still present at both the cranio-cervical junction and lower neck after 12 months. The most significant symptoms are related to instability at the cranio-cervical junction. This level of injury is fortunately not found in other volunteer whiplash testing because the acceleration pulse is deliberately kept at a much lower level: 4.9–13.7 ms⁻² [26, 27]. This case therefore affords a unique opportunity to compare actual high-energy real-life whiplash injuries with well documented biomechanics.

It is impossible to relate individual injury locations directly to either frontal or rear impacts since both were undertaken. Further, it is possible that injuries created in the initial impact were further aggravated by the later one.

Whilst not planned when designing the impact rig, the sled impact pulses are not dissimilar to those used in EuroN-CAP whiplash tests (which use the BioRID dummy) High (Fig. 13) and Medium (Fig. 14) severity pulses corridors [30].

Good correlation was observed between the experiment and model for the motions of the head and shoulder for both the frontal and rear-end collisions (Figs. 3, 4) during the impact phase (0–160 ms). This gives confidence in the predictions of the model for parameters, such as segmental shear, that cannot be observed in the experiment. Similarly, the magnitudes of the injury criteria and C0–C2 translations are very similar to a study using crash test dummies performed using similar boundary conditions [31]. The authors recognize that this is not a perfect validation and recommend caution when interpreting the model predictions. We therefore have limited discussion of these results to whether or not injury thresholds were exceeded.



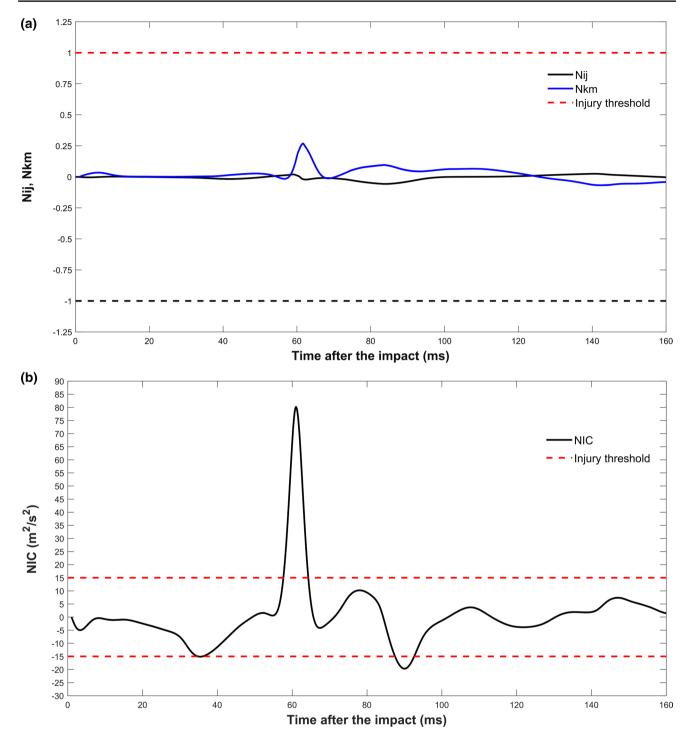


Fig. 10 Neck injury criteria, Nij and Nkm (a), NIC (b) and IV-NIC (c) during the simulation of the rear collision

The most significant clinical finding was an injury at the cranio-cervical junction, however this was not predicted by either of the standard upper neck injury criteria, Nij and Nkm. Indeed, both parameters remained considerably below threshold levels. However, in both the frontal

and rear collisions the antero-posterior acceleration of C0–C2 was predicted to be considerably higher (11–40 g) compared to the injury threshold for the alar ligaments (8 g) proposed by Maak [25]. It should be noted that these peak accelerations corresponded to direct impacts of the



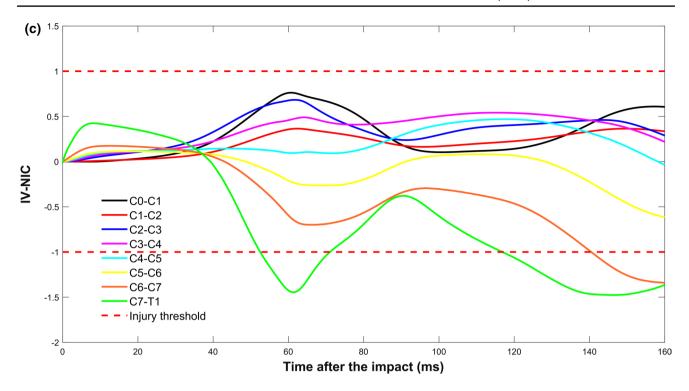


Fig. 10 (continued)

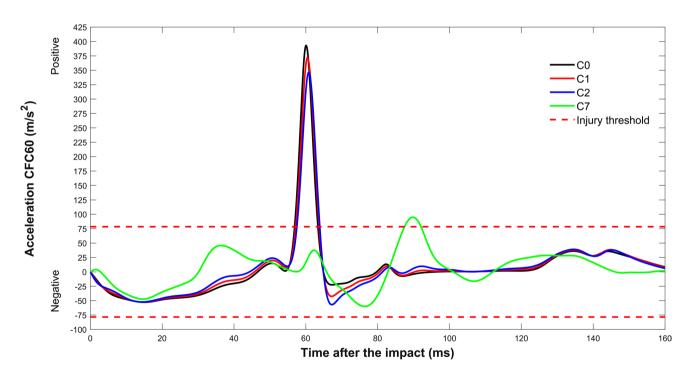


Fig. 11 Acceleration of the vertebrae in the direction of the X-axis during the simulation of the rear-end collision

head on the chest or headrest and were of short duration (approximately 10 ms). Similarly, 15 mm anterior shear of the skull relative to C2 was predicted for the frontal

collision. This supports the hypothesis that this impact might lead to damage to the alar ligaments.



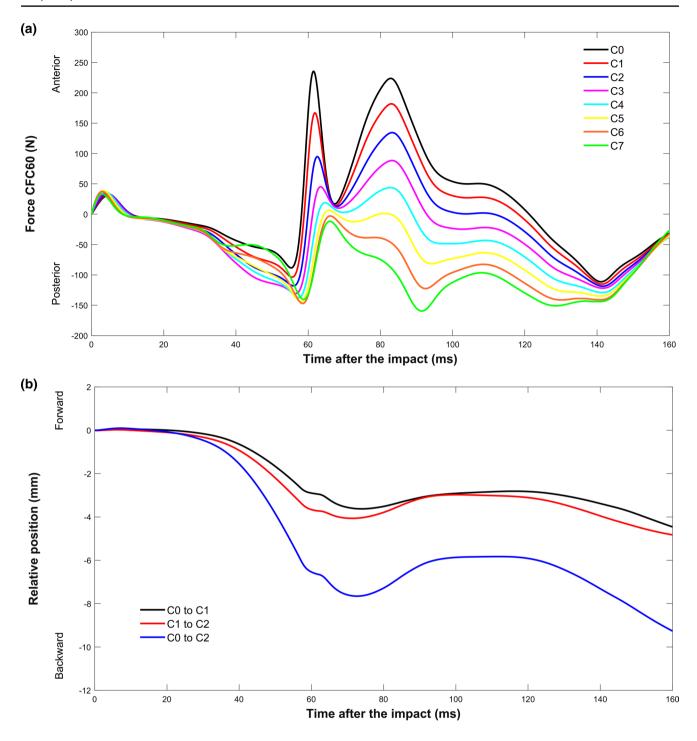


Fig. 12 Antero-posterior forces (a) acting on the vertebrae of the cervical spine and the resulting displacements (b) in the simulation of the rear collision

These findings suggest that the clinical observation of significant cranio-cervical instability may be due to damage of the alar ligaments caused by excessive anterior acceleration and/or anterior shear at this section of the spine. They further suggest that the conventional upper neck injury criteria, Nij and Nkm, are not the best

parameters to predict such injuries and that relative acceleration (or motion) between C0 and C2 should be used instead.

Beyond the cranio-cervical junction injury, considerable clinical disruption was also observed throughout the neck and particularly at the C6–T1 levels. These findings



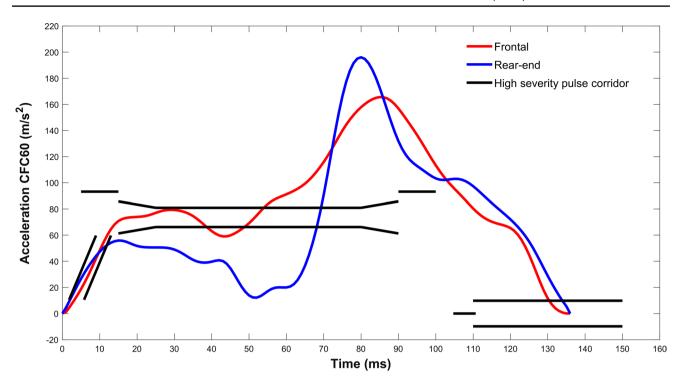


Fig. 13 Comparison of the frontal and rear-end crash pulses with EuroNCAP High severity pulse

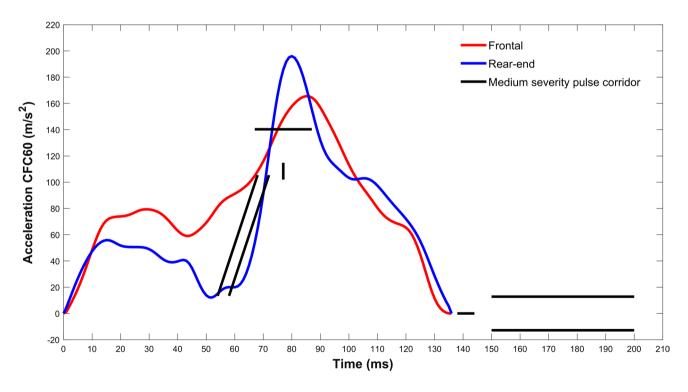


Fig. 14 Comparison of the frontal and rear-end crash pulses with EuroNCAP Medium severity pulse

correspond well with the peak values of NIC for both the frontal and rear impacts; both of which (17 and 80 vs. $15 \text{ m}^2\text{s}^{-2}$) exceeded the injury threshold. It is possible to

explore this further at a segmental level using the IV-NIC criterion by normalizing the predicted flexion/extension angles with normal ranges of motion under physiological



Table 1 Maximum intervertebral flexion angles under physiological loadings compared with those during the simulated frontal collision in MADYMO

Level	C3-C4	C4-C5	C5-C6	C6-C7	C7-T1
Physiological ROM	4.2	4.8	5.8	4.5	2.1
Peak flexion	5.9	10.1	11.6	11.3	6.9
IV-NIC	1.4	2.1	2.0	2.5	3.3

loadings [5]. It can be seen from Table 1 that the normal physiological ROM was exceeded at all levels but particularly at the base of the neck.

NIC, a measure of overall deformation of the neck, therefore seems to be a good predictor of generalized neck injury and this is supported by the intersegmental hyperflexion injury criterion, IV–NIC, which provides the further insight that hyperflexion injury is more likely (and more sever) from the cranial to caudal.

The model is sensitive to its boundary conditions, e.g. amplitude of acceleration pulses, properties of the seat and seatbelt materials, initial positions of the head and neck, stiffness of joints. Choices had to be made in terms of the values used for these parameters and these choices limit the applicability of the model. This is particularly the case in terms of the seatbelt materials and initial subject position which were chosen to match the experimental case. Similarly, the joint and inertial properties of the model human, whilst well validated to a 50th percentile male human, are those of this sized person. To examine the effect of acceleration pulse, the simulations were repeated with acceleration pulse at $\pm 10\%$. The results of these simulations complied with our previous conclusions about the results. A further limitation of the study is that during the recording of videos the volunteer was aware that the impact will occur within moments. This might lead to changes in the muscle tone of his neck, resulting in a more intentional reaction. It was not possible to evaluate the state of awareness of the volunteer from the videos, especially for the rear-end collision. Therefore, in this study an unaware muscle activation condition was simulated, with the motion of MADYMO human model during the simulations determined only by externally applied forces (sled acceleration pulse and gravity acceleration) and restricted by the seat and seatbelt.

Conclusions

 We present a unique case of a high energy frontal and rear whiplash events where the motion of the subject was recorded using high speed video allowing the validation of a specific computation model of segmental level kinetic and kinematics of the collision.

- The severity of the frontal and rear crash acceleration pulses was similar to those used in the EuroNCAP whiplash tests.
- The criteria used by the automotive industry standard surrogates for upper neck injury (Nij and Nkm) did not predict the significant cranio-cervical junction injury observed clinically.
- The cranio-cervical junction injury was predicted by both anterior acceleration and C0–C2 shear displacement values.
- Overall and particularly lower neck hyperflexion injury was predicted by the NIC and IV–NIC injury criteria.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00586-021-06851-y.

Declarations

Conflict of interest The authors have no conflict of interest.

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