The probability of traumatic brain injuries based on tissue-level reliability analysis

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Purpose: Motor vehicle crashes are one of the leading causes of traumatic brain injuries. Restraint systems of cars are evaluated by crash tests based on human tolerance data, however, the reliability of data currently used has been questioned several times in the literature due to the neglect of certain types of effects, injury types and uncertainties. Our main goal was to re-evaluate the currently applied risk curve by taking the previously neglected effects into account. *Methods*: In this paper, the probability of traumatic brain injury was determined by reliability analysis where different types of uncertainties are taken into account. The tissue-level response of the human brain in the case of frontal crashes was calculated by finite element analyses and the injury probability is determined by Monte Carlo simulations. Sensitivity analysis was also performed to identify which effects have considerable contribution to the injury risk. *Results*: Our results indicate a significantly larger injury risk than it is predicted by current safety standards. Accordingly, a new risk curve was constructed which follows a lognormal distribution with the following parameters: $\mu_{LN} = 6.5445$ and $\sigma_{LN} = 1.1993$. Sensitivity analysis confirmed that this difference primarily can be attributed to the rotational effects and tissue-level uncertainties. *Conclusions*: Results of the tissue-level reliability analysis enhance the belief that rotational effects are the primary cause of brain injuries. Accordingly, the use of a solely translational acceleration based injury metric contains several uncertainties which can lead to relatively high injury probabilities even if relatively small translational effects occur.

Key words: traumatic brain injuries, finite element simulations, reliability analysis, Head Injury Criterion, injury risk curves

1. Introduction

Traumatic brain injuries (TBIs) have a devastating epidemiological importance, since they contribute to the mortality and morbidity in the society with a significantly large extent. In the United States 1.7 million people suffer a TBI and 52,000 die among them every year [3], moreover, the cost of these injuries has been estimated at 56.3 thousand million dollars, implying that the treatment and rehabilitation of injured people cause a considerate economic burden to the society. Motor vehicle crashes are one of the leading causes of TBIs, therefore, the prevention of these injuries is a major concern in the automotive industry. It can be possible thanks to improved passive restraint systems which guarantee that the risk of

TBIs has a relatively low, acceptable value. Applied restraint systems are evaluated by crash tests, where a representative value of the loading conditions occurring on the head of dummies (i.e., effect) is calculated and compared to a threshold value (i.e., resistance). Such thresholds are taken from risk curves where the conditional probability of injury is given in the function of the effect, therefore, the rigorousness of the applied safety standards highly depends on the reliability of the considered risk curve. Currently, safety standards of automotive industry (e.g., Federal Motor Vehicle Safety Standard (FMVSS 208), European Directive (ECE R94), etc.) are based on the Head Injury Criterion (HIC) [24] where the magnitude of the loading effect is characterized by a HIC value calculated as the maximum value of the following integral:

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HIC =
$$\left[\frac{1}{t_2 - t_1} \int_{t_1}^{t_2} a(t) dt\right]^{2,5} (t_2 - t_1)$$
 (1)

where a(t) is the measured resultant instantaneous linear acceleration at the centre of gravity of the head and $t_2 - t_1$ is the time interval which is chosen to maximize HIC.

Ever since its adaption into the FMVSS 208 in 1972, several doubts exist in the biomechanical community with regards to the application of HIC [15]. A major concern is that HIC takes into account only the effect of translational accelerations acting on the head, and neglects the effect of rotational accelerations which can have an even larger role in the occurrence of TBIs [5], [17], [25]. Another main critic of HIC is that it considers only the external kinematic effects acting on the human head, thus neglects the response of the soft and highly deformable brain tissue [7].

Further critics exist regarding the applied threshold value of HIC. According to the FMVSS 208 and ECE R94 standards, HIC is calculated by considering a 15 ms long time interval in Eq. (1) and this value (HIC_{15}) is related to the conditional probability of a severe (AIS4+ according to the Abbreviated Injury Scale) injury ($P_{AIS4+|HIC_{15}}$) in the following way [18], [12]:

$$P_{\text{AIS4+}|HIC_{15}} = \Phi\left(\frac{HIC_{15} - 1434}{430}\right),$$
 (2)

where Φ is the cumulative standard normal distribution function. In the case of standardized frontal crash tests, the threshold value applied in the above-mentioned standards is $HIC_{15} = 700$, which belongs to 5% probability of injury according to Eq. (2). This observation is based on cadaver experiments where the occurrence of skull fracture and hematoma were investigated, while other types of TBI were not taken into account.

The comparison of TBI risk obtained by observations of real-world crashes and the risk which is predicted by standards corresponding to well-controlled tests is a difficult task, because several discrepancies may exist in the impact conditions. Nevertheless, Mueller et al. [14] found that HIC may seriously underestimate the injury probability in the case of small and moderate overlap frontal crashes, since the predicted $P_{\text{AIS4+}|HIC_{15}}$ was less than one-tenth of the observed value.

Due to the above-mentioned critics, many other criteria have been proposed, but the attempt to replace HIC has been unsuccessful so far, thus HIC seems to stay a widely applied injury indice in the close future. Recently, the Brain Injury Criterion (BrIC) has been

developed [23], which serves as an extension beside HIC, however, investigations [19], [14] showed that the injury risk estimated by BrIC could be much higher than its observed value (which is based on real-world crashes), thus further research is necessary.

An advanced vulnerability analysis of the human brain should involve the detailed description of the tissue-level response (i.e., values and distribution of the occurred strains, stresses and pressure) of the brain. Currently, the most widely used trend is to determine these tissue-level effects via finite element (FE) simulations [7], [21], [8], [23] and compare them to tissue-level resistances. Such tissue-level thresholds of humans can be estimated by finite element reconstructions of real-world injuries [7], [8], animal experiments after using certain scaling methods [21] and experiments performed on cell cultures [9].

The main goal of the current research is to investigate the connection between HIC_{15} and $P_{AIS4+|HIC_{15}}$ corresponding to frontal crash tests performed with the standardized 56 km/h impact velocity. Based on the above-mentioned investigation of real-world crashes [14] and the fact that several effects were neglected during the development of HIC and the currently used risk curve (defined by Eq. (2)), it is hypothesized that the risk may be considerably larger than it is predicted by current standards.

In reliability engineering, one of the main tasks of risk analysis is the characterization of different types of uncertainties which can significantly influence the probability of failure. In our case, a major source of uncertainties may exist due to the variability of the tissue-level resistance among humans. Furthermore, it is hypothesized that even if the acceleration loading curves belong to the same HIC_{15} value, tissue-level effects may have a relatively large variability among crashes due to the following reasons:

- several types of uncertainties can affect the accelerations which occur on the human head during a car crash.
- HIC neglects the effect of rotational accelerations and the response of the brain tissue.

Obviously, further sources of uncertainties also exist, and characterization of them requires further research which is out of the scope of this paper.

Corresponding to other engineering fields, reliability analysis [16] is considered as a state-of-art tool of risk analysis which can be applied to perform an advanced vulnerability assessment of the analysed system. In this case, each type of uncertainties can be taken into account via random variables defined by their distribution function. Analogously, this method could also be applied in the case of the human brain,

where different injury types are considered as failure components described by limit-state functions [4].

2. Methods

In order to investigate the $HIC_{15} - P_{AIS4+|HIC_{15}}$ connection, the probability of traumatic brain injury was determined for several HIC_{15} values by reliability analysis using Monte Carlo (MC) simulations [20]. This approach enabled us to construct a new risk curve which can be used to re-evaluate the validity of the currently applied risk curve which is given by Eq. (2). Considering the above-mentioned critics, the reliability analysis performed in this paper met the following requirements:

- Injury criteria were described at tissue-level.
- Tissue-level effects were calculated via a finite element model which has already been validated and used in previous research.
- Certain types of uncertainties which can affect injury probability significantly were taken into account by random variables.

An AIS4+ injury can occur with different types of brain lesion, which should be taken into account during the reliability analysis. In accordance with previous research [21], the following three of the most common types of TBI were considered in this paper:

- diffuse axonal injury (DAI),
- acute subdural hematoma (ASDH),
- contusion.

During the reliability analysis, each injury type is represented as a failure component described by the following G_i (i = 1, ..., 3) limit-state functions (where i = 1 belongs to DAI, i = 2 belongs to ASDH and i = 3 belongs to contusion):

$$G_1 = R_{CSDM} - E_{CSDM} , (3a)$$

$$G_2 = R_{RMDM} - E_{RMDM}, (3b)$$

$$G_3 = R_{DDM} - E_{DDM} \,, \tag{3c}$$

where R_{CSDM} , R_{RMDM} and R_{DDM} are random variables describing tissue-level resistances in terms of cumulative strain damage measure (CSDM) (with strain threshold equal to 0.15), relative motion damage measure (RMDM) and dilatational damage measure (DDM) which are detailed in [21]. These variables are characterized based on figures provided in [21], and the applied distribution types and parameters (μ_R and σ_R) are summarized in Table 1.

Table 1. Random variables describing the tissue-level resistance

Random variable	Distribution type	$\mu_{ m R}$	σ_R	
R_{CSDM}	normal	0.55	0.3	
R_{RMDM}	normal	1	0.35	
R_{DDM}	lognormal	-2.8811	0.7072	

In Eq. (3) E_{CSDM} , E_{RMDM} and E_{DDM} are random variables which represent the stochastic nature of tissue-level effects. In order to determine tissue-level effects corresponding to a given test, the concept introduced by Takhounts et al. [21] was applied. Namely, the accelerations measured on the head of an advanced anthropomorphic test dummy (AATD) were applied to obtain loading time histories to a finite element model of the head. Although the kinematic properties of test dummies somewhat differ from humans', AATDs are widely used in the automotive industry to evaluate the occupant protection potential of new vehicles [13]. In order to get reliable kinematic data, the Hybrid III type dummies which have excellent biofidelity and measurement capabilities have been used in frontal crash tests since 1986 [13]. Translational accelerations in several locations and directions on the dummies' head were measured by a Nine Acceleration Array Package (NAAP) [22], and rotational accelerations were computed from the measured linear accelerations in Simulated Injury Monitor (SIMon) software [21] based on the rigid body dynamics of the human skull. In the knowledge of the translational and rotational accelerations which occurred on the dummies' head, tissue-level effects were calculated by the finite element head model, included in the SIMon software (Fig. 1). During the simulations of frontal

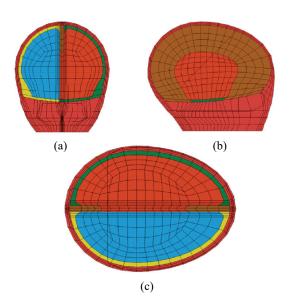


Fig. 1. SIMon's finite element model of the human head: (a) coronal section, (b) sagittal section, (c) axial section

crashes a 56 km/h initial velocity of the human head was prescribed. Afterwards, load curves (i.e., time vs. velocity functions) were computed in SIMon (based on the measured translational accelerations which act on the rigid skull, whose movement affects the motion of the brain due to the implemented tie-break contacts.

In order to characterize the uncertainty of tissue-level effects, a set of realistic acceleration records were required to take into account the natural variability of acceleration time histories and the ratio of the translational and rotational effects. Furthermore, these records should represent the same HIC₁₅ value during the calculation of $P_{\text{AIS4+}|\text{HIC}_{15}}$ to avoid any bias due to different loading intensities, therefore this procedure required the selection and scaling of acceleration records. Accordingly, 100 frontal crash tests which met the following requirements were selected randomly from the National Highway Traffic Safety

Administration (NHTSA) database:

- the crash test was performed with 56 km/h impact velocity,
- the car crashed into a rigid barrier,
- airbags were built in the car,
- the Hybrid III type dummy was applied,
- accelerations on the dummies' head were measured by a Nine Acceleration Array Package.

Statistical parameters of the measured HIC_{15} values corresponding to the selected crash tests are summarized in Table 2.

In order to calculate $P_{\rm AIS4+|HIC_{15}}$ for several HIC_{15} value, the measured nine translational acceleration records of selected crash tests were scaled linearly by a scaling factor calculated for each test respectively, ensuring that all 100 tests represent the desired HIC_{15} value. Based on rigid body dynamics of the human skull, the scaling of translational accelerations causes

Table 2. Statistical parameters of the one hundred HIC_{15} values observed during the selected crash tests (μ – mean value, σ – standard deviation, CoV – coefficient of variation, η – skewness, κ – kurtosis, HIC_{\min} – minimum value, HIC_{\max} – maximum value)

μ	σ	CoV	η	К	HIC_{\min}	HIC_{max}
315.66	124.82	0.3954	0.9087	3.3492	107.12	659.91

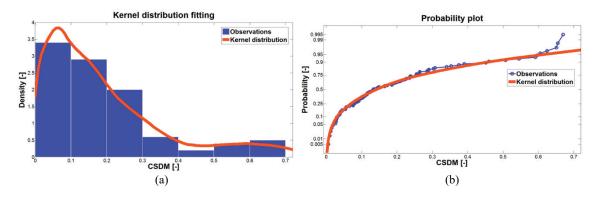


Fig. 2. Kernel density estimation of E_{CSDM} in case of $HIC_{15} = 700$: (a) fitting density function to the histogram of the observed data, (b) checking of the curve fitting by probability plot

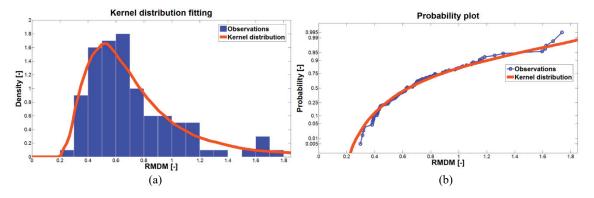


Fig. 3. Kernel density estimation of E_{RMDM} in case of $HIC_{15} = 400$: (a) fitting density function to the histogram of the observed data, (b) checking of the curve fitting by probability plot

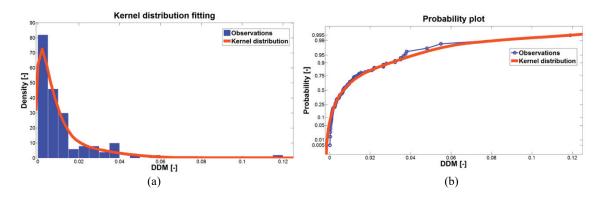


Fig. 4. Kernel density estimation of E_{DDM} in case of $HIC_{15} = 1500$: (a) fitting density function to the histogram of the observed data, (b) checking of the curve fitting by probability plot

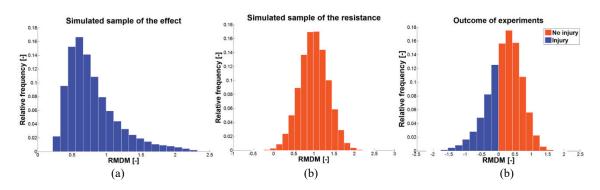


Fig. 5. Illustration of Monte Carlo simulation:
(a) random sample of the effect, (b) random sample of the resistance, (c) outcome of experiments

the scaling of the rotational accelerations as well. Tissue-level effects were calculated at eight different HIC_{15} levels (HIC_{15} equals 200, 400, 500, 600, 700, 1000, 1500 and 2000) by the SIMon software.

After performing the finite element simulations, at each HIC_{15} level the obtained 100 realizations of the tissue-level effects were considered as statistical samples used for the characterization of E_{CSDM} , E_{RMDM} and E_{DDM} variables. In certain cases, parametric distributions could not be reliably fitted to the observed data, therefore curve fitting was performed by non-parametric kernel density estimation in Matlab environment [11] using $Epanechnikov\ kernels$ [2] (Figs. 2a, 3a, 4a). The curve fitting of distribution functions was checked qualitatively by the probability plot method (Figs. 2b, 3b, 4b).

Conditional injury probability $P_{\text{AIS4+}|HIC_{15}}$ corresponding to the G_i limit-state function was calculated by Monte Carlo simulations where 10^6 random samples of tissue-level effects (Fig. 5a) and resistances (Fig. 5b) were generated according to their distribution function in Matlab. The outcome of the 10^6 virtual experiments was evaluated according to Eq. (3) respectively, where negative values of G_i indicated injurious and

non-negative values indicate non-injurious outcomes (Fig. 5c).

After the evaluation of virtual experiments, the conditional injury probability was calculated in the following way:

$$P_{AIS4+|HIC_{15},i} = \frac{\text{number of experiments when injury occurred}}{\text{number of experiments}}. (4)$$

In order to ensure that the uncertainty of effect was characterized reliably, a convergence check was performed, where the variability of the calculated $P_{\text{AIS4+}|\text{HIC}_{15,i}}$ values was observed in the function of the number of the considered crash tests (Fig. 6).

Converge analysis (Fig. 6) showed that in the case of the consideration of at least 80 crash tests, the relative error of the calculated injury probability is within 1-5%. This magnitude of uncertainty is considered to be admissible, thus 100 crash tests are reconstructed by FE simulations at the above-mentioned HIC_{15} levels.

In the knowledge of $P_{AIS4+|HIC_{15},i}$ for each analysed injury type, the probability of an AIS4+ injury can be

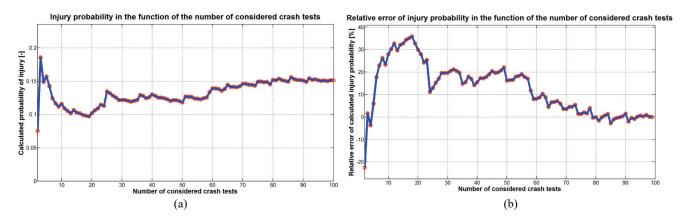


Fig. 6. Results of convergence check: (a) convergence of $P_{AIS4+|HIC_{15}=700,1}$, (b) relative error of the results (the same calculation was conducted in case of each $P_{AIS4+|HIC_{15},i}$ result and approximately the same magnitude of errors has been observed)

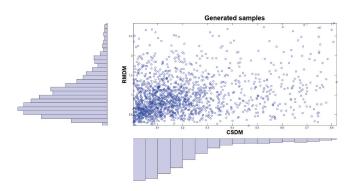


Fig. 7. Generated sample of the effect in case of $HIC_{15} = 700$ with non-parametric marginal distributions of E_{CSDM} and E_{RMDM}

determined by the reliability analysis of the system, which consists of the above-mentioned three failure components. These components form a so-called series system considering that the occurrence of one injury type already causes an AIS4+ injury. Accordingly, an estimation of the system reliability could be given via simple lower and upper bounds as shown in Eq. (5).

$$\max(P_{AIS4+|HIC_{15},i}) \le P_{AIS4+|HIC_{15}} \le \sum_{i=1}^{3} P_{AIS4+|HIC_{15},i}$$
 (5)

Afterwards, the reliability of the system was evaluated by Monte Carlo simulations where 10⁶ random samples (i.e., random vectors with three components) of the effect and the resistance were generated according to their multivariate distribution function. During the construction of these functions the same Kernel-type non-parametric marginal distribution functions were applied as earlier. In order to take into account the correlation, multivariate copula functions were used to generate correlated vector components [10] of the effect (Fig. 7).

Correlations between E_{CSDM} , E_{RMDM} and E_{DDM} were estimated based on the results of the corresponding FE

simulations by the Kendall-type rank correlation coefficient [6] which is invariant to the nonlinear inverse transformations applied during the Monte Carlo simulations. Since multivariate distribution functions are not uniquely defined by their marginal distributions and their correlation, calculations were performed with several types of copula functions (Gaussian and *t* copulas with different number of parameters) to analyse the sensitivity of the results.

In the knowledge of $P_{\text{AIS4+}|HIC_{15}}$ for several HIC_{15} values, a new risk curve was constructed by curve fitting performed by the least square method.

Following our first hypothesis that injury risk could be considerably larger due to rotational acceleration and uncertainties than it was predicted earlier, a sensitivity analysis was carried out to evaluate the contribution of different factors to the injury risk. Accordingly, calculations were repeated with the neglect of (i) the uncertainties of the resistance, and (ii) the rotational effects, respectively. The first one was achieved by setting the σ_R parameter of R_{CSDM} , R_{RMDM} and R_{DDM} to zero, while the latter – by running new FE simulations with the modification of the time vs. rotational velocity functions (i.e., three load curves)

to constant zero functions, as it was applied in [1]. Obviously, these were unrealistic "what if" scenarios (since rotational effects always occur with a certain magnitude), nonetheless they represented realistic translational effects with the given HIC_{15} intensity, thus they were used to analyse theoretically what would happen if rotational effects did not occur.

3. Results

Statistical parameters of the 100 realizations of effects obtained by FE simulations are summarized in Table 3.

Following the above-mentioned steps, results of conditional injury probabilities and the reliability of the system are summarized in Table 4.

It is mentioned that the reliability of the system has a negligible variability (CoV < 0.01) when the calculations are repeated with the above-mentioned different types of copula functions, thus only results obtained by Gaussian copulas are shown in Table 4.

Based on results of MC, modified risk curve can be fitted to $HIC_{15} - P_{AIS4+|HIC_{15}}$ pairs. Since current results show a relatively large injury probability in the $HIC_{15} = 0$ –1000 interval (Table 4), a fitted normal distribution function would predict an unrealistically large injury probability for $HIC_{15} \approx 0$ (and even for

Table 3. Statistical parameters of the results of FE simulations (μ = mean value, σ = standard deviation, CoV= coefficient of variation, η = skewness, κ = kurtosis, r= range)

					•		
Effect	HIC ₁₅	μ	σ	CoV	η	К	r
CSDM		0.0229	0.0312	1.3640	2.9917	12.2703	0.1687
RMDM	200	0.5313	0.2365	0.4452	1.3667	4.7314	1.0969
DDM		0.0002	0.0009	3.8452	5.9962	39.4443	0.0065
CSDM		0.0886	0.1326	1.4967	3.7533	21.0841	0.9586
RMDM	400	0.7190	0.3176	0.4417	1.3178	4.5203	1.4406
DDM		0.0008	0.0020	2.3948	3.5701	16.2403	0.0121
CSDM		0.1107	0.1175	1.0615	1.9920	6.4451	0.5091
RMDM	500	0.7937	0.3483	0.4388	1.3550	4.6425	1.5756
DDM		0.0016	0.0033	2.0906	3.2345	13.3094	0.0179
CSDM		0.1394	0.1427	1.0234	1.9396	6.2889	0.6189
RMDM	600	0.8419	0.3721	0.4420	1.3412	4.6517	1.7034
DDM		0.0023	0.0048	2.1311	3.9105	21.0107	0.0330
CSDM		0.1911	0.1644	0.8600	1.4030	4.3401	0.6645
RMDM	700	0.9256	0.4021	0.4344	1.3345	4.5826	1.8175
DDM		0.0056	0.0189	3.3961	6.6789	51.2671	0.1620
CSDM		0.2910	0.1934	0.6645	0.9679	3.6192	0.8486
RMDM	1000	1.0947	0.4827	0.4409	1.3895	4.9153	2.3873
DDM		0.0079	0.0177	2.2534	6.4571	53.5886	0.1590
CSDM		0.4074	0.2121	0.5205	0.2020	2.5029	0.8708
RMDM	1500	1.2980	0.6117	0.4713	1.5449	5.5343	3.2365
DDM		0.0115	0.0156	1.3531	3.8092	23.8863	0.1189
CSDM		0.5392	0.2133	0.3956	-0.2388	2.3545	0.8795
RMDM	2000	1.5732	0.7041	0.4475	1.6331	6.0198	3.7435
DDM		0.0171	0.0153	0.8904	1.4425	4.5870	0.0725

Table 4. Injury probabilities obtained by reliability analysis

HIC ₁₅	$P_{ ext{AIS4+} HIC_{15},1}$	$P_{\mathrm{AIS4+}\mid HIC_{15},2}$	$P_{\mathrm{AIS4+}\mid HIC_{15},3}$	Lower bound of $P_{AIS4+ HIC_{15}}$	Upper bound of $P_{\text{AIS4+} HIC_{15}}$	$P_{\text{AIS4+} HIC_{15}}$ based on system reliability
200	0.0409	0.1410	≈0	0.1410	0.1819	0.1810
400	0.0800	0.2639	0.0003	0.2639	0.3442	0.3279
500	0.0915	0.3165	0.0015	0.3165	0.4095	0.3806
600	0.1131	0.3469	0.0041	0.3469	0.4641	0.4234
700	0.1515	0.4075	0.0236	0.4075	0.5826	0.4993
1000	0.2346	0.5186	0.0310	0.5186	0.7842	0.6179
1500	0.3509	0.6273	0.0527	0.6273	1	0.7326
2000	0.4920	0.7648	0.0944	0.7648	1	0.8438

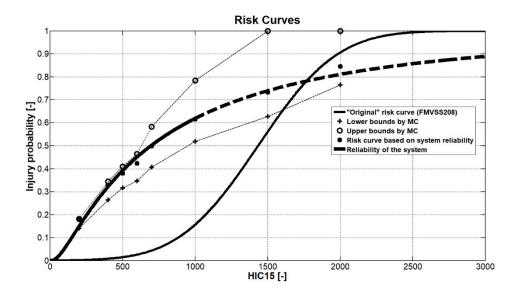


Fig. 8. Modified risk curve obtained by reliability analysis

Table 5. Parameters of the obtained injury risk curve

Distribution type	μ_{LN}	σ_{LN}		
Lognormal	6.5445	1.1993		

Table 6. Results of the sensitivity analysis

HIC ₁₅	P _{AIS4+ HIC₁₅} without the uncertainties in the resistance	$P_{{\rm AIS4+} HIC_{15}}$ without rotational effects
200	0.0777	0.0064
400	0.2024	0.0110
500	0.2559	0.0142
600	0.3057	0.0165
700	0.3876	0.0219
1000	0.5253	0.0322
1500	0.6755	0.0718
2000	0.8277	0.1159

negative HIC_{15} values). Therefore, the use of a lognormal distribution function was proposed here as a more appropriate base function for the curve fitting. Parameters of the new risk curve obtained by the least square method are summarized in Table 5 and corresponding risk curves are shown in Fig. 8.

Results of the sensitivity analysis in terms of $P_{\text{AIS4+}|HIC_{15}}$ are summarized in Table 6.

It could be seen in Table 6 that relatively small injury probabilities are obtained when rotational effects are neglected. These low probability values have a relatively good correspondence with the original risk curve in the $HIC_{15} = 0$ –700 interval. These relatively low $P_{\text{AIS4+}|HIC_{15}}$ values are almost equal with the corresponding $P_{\text{AIS4+}|HIC_{15},2}$ result, since the injury probability of DAI and contusion tended to zero. It might not be surprising considering that DAI is a diffuse type of injury which is thought to be caused by rotational effects [1], [7], while the analysis of contusion re-

Table 7. Statistical parameters of *RMDM* results of FE simulations without rotational effects $(\mu = \text{mean value}, \sigma = \text{standard deviation}, CoV = \text{coefficient of variation}, \\ \eta = \text{skewness}, \kappa = \text{kurtosis}, r = \text{range})$

HIC_{15}	μ	σ	CoV	η	κ	r
200	0.1133	0.0523	0.4614	2.6291	11.9945	0.3330
400	0.1768	0.0706	0.3992	1.9620	8.4694	0.4180
500	0.2042	0.0789	0.3863	1.5781	6.7294	0.4608
600	0.2200	0.0862	0.3920	1.5680	7.9149	0.5300
700	0.2525	0.1010	0.3999	1.0265	5.3622	0.5964
1000	0.3081	0.1125	0.3650	1.1660	5.5205	0.6441
1500	0.4229	0.1571	0.3714	0.9921	4.6799	0.8743
2000	0.5124	0.2045	0.3991	1.1207	4.8750	1.1458

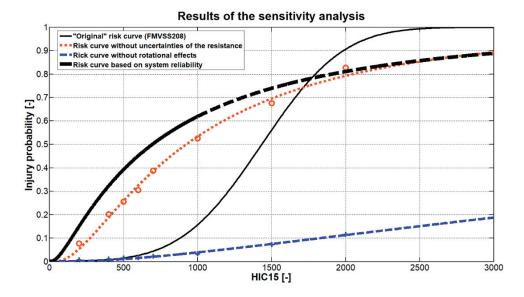


Fig. 9. Risk curves based on the results of the sensitivity analysis

sulted in relative small probabilities even if rotational effects were present (Table 4). Therefore, only tissue-level effects obtained during the analysis of ASDH (without rotational effects) are summarized in Table 7.

Risk curves were fitted to the results of the sensitivity analysis as well. These curves are shown in Fig. 9 in addition to the "original" and the new risk curve.

4. Discussion

In this paper, the vulnerability assessment of the human brain was performed by reliability analysis, in order to estimate the probability of traumatic brain injuries in the case of frontal car crashes, by taking into account certain types of uncertainties of the effect and resistance. It was hypothesized that injury risk may be considerably larger than it is predicted by current safety standards, since during the construction of the original risk curve certain injury types and uncertainties corresponding to the kinematic effects had been neglected. Our results (Table 4 and Fig. 8) support this hypothesis, since injury probability for $HIC_{15} = 700$ obtained by MC is 0.4993 instead of 0.05 which was predicted by the "original" risk curve. Even for $HIC_{15} = 500$, injury probability obtained by MC is significant (0.3806), while in the case of $HIC_{15} = 1000$, the 50% of injury probability was already exceeded (0.6179). Based on these results, a new risk curve was constructed (Table 5, Fig. 8) by the least square method where the application of a lognormal distribution function was more suitable than the normal distribution function used earlier.

The observed difference between the risk curve obtained by reliability analysis and the "original" risk curve (defined by Eq. (2)) can be attributed to several reasons. Basically, during the reliability analysis certain types of effects and uncertainties were taken into account which had not been considered earlier, thus the new risk curve corresponds to a relatively large total uncertainty (which is quantified in Table 5 by σ_{LN}). The magnitude of this total uncertainty is highly responsible for the shape of the obtained risk curve and the observation that the predicted injury probability is significantly larger in the $HIC_{15} = 0-1000$ interval than it was predicted earlier. These results can be interpreted in a way that, since during the application of HIC metric several effects and uncertainties were neglected, a considerable injury probability is present even if relatively small HIC₁₅ belongs to a crash. Accordingly, it was shown in Table 3 that a relatively large variability of tissue-level effects could be observed due to complex kinematic effects including rotational accelerations and velocities, even if the same HIC_{15} value belonged to the tests. For instance, in the case of ASDH – which is predicted to be the most significant injury type (Table 4) – the CoV of RMDM is between 0.4344 and 0.4713, while in the case of DAI and contusion the CoV of the corresponding tissue-level effect is even larger.

Sensitivity analysis has shown that the *CoV* of *RMDM* is slightly smaller (it is between 0.3650 and 0.4614) if rotational effects are not in present. However, its mean value is significantly less in this case (Table 7), which indicates that relatively small injury probabilities would exist if rotational effects did not occur (Table 6). The effect of rotational accelerations

is illustrated in Fig. 9 in terms of risk curves. These results strengthen the belief that rotational effects are the primary cause of brain injuries [1], [7]. Accordingly, it might not be so surprising that the use of a solely translational acceleration-based injury indice includes several uncertainties which can lead to relatively high injury probabilities even if relatively small translational effects occur. It seems to be the case, considering that the knowledge of the HIC_{15} value of a test do not characterize how large rotational effects occurred, and these governing effects with their "uncharacterized magnitude" may cause much more serious consequences than the translational effects do.

Furthermore, a relatively large uncertainty can be observed corresponding to tissue-level tolerances of humans since the applied resistance models (Table 1) work with CoV = 0.35–0.806. Sensitivity analysis has also shown (Table 6, Fig. 9) that these uncertainties are partially responsible for the relatively high injury probabilities which were observed in the $HIC_{15} = 0$ –1000 interval, however, this contribution is considerably smaller than the contribution of rotational effects as it was mentioned above.

Moreover, our results (Table 4) suggest that a significant injury probability (e.g., 15.15% for $HIC_{15} = 700$) belongs to the occurrence of DAI and a moderate injury probability (e.g., 2.36% for $HIC_{15} = 700$) for contusion. These injury types were not taken into account during the construction of the "original" risk curve, hence this neglect can be also partially responsible for the observed differences.

The construction of the "original" risk curve was based on cadaver experiments [18] where different impact velocities and impact conditions were applied (e.g., head drop tests on flat, rigid and padded surfaces, cadaver sled tests against windshield; drop tests of helmeted cadavers). Since these impact conditions and velocities could be different from those which occur during the analysed car crashes, this discrepancy may also contribute to the differences between the "original" and our modified risk curve (Fig. 8).

Although the comparison of TBI risk observed in real-world crashes and predictions based on standardized tests may not be so reliable, current results of the tissue-level reliability analysis support previous real-world observations [14], where it was found that HIC may significantly underestimate injury risk. However, this comparison has the limitation that Mueller et al. [14] considered small and moderate overlap frontal tests which had been performed with 64 km/h impact velocity.

As a limitation of our results it is mentioned that while certain types of uncertainties were considered during the reliability analysis, there are further sources of uncertainties whose investigation should be the topic of further research. For instance, uncertainties corresponding to the finite element modelling and the statistical process of observed results should be taken into account in the future, however, the consideration of these so-called epistemic uncertainties is not so straightforward, and it is still the topic of active research. Moreover, the natural variability of geometric and kinematic characteristics among humans can influence the kinematic effects occurring on the head, therefore its characterization could be an interesting task in the future.

A limitation of our study comes from the application of the 2003 version of the SIMon head model. Tissue-level results are always sensitive to the applied model, thus it was convenient to apply the same model for characterizing tissue-level effects which was used earlier to determine the resistances. The original aim of the authors of the model was to reduce complexity in order to obtain a reasonable simulation time without sacrificing the accuracy of the injury prediction. Although this model included only the most essential anatomic parts, it went through a rigorous validation procedure [21] where the relative motion of the brain with respect to the skull was compared to results of cadaver experiments. In our case it was very convenient to use this simplified model for the large number of simulations, however, as the hardware capacities increase in the close future, it would be interesting to perform such simulations with more advanced models where further geometric details (e.g., gyri, sulci, distinguish of white and grey matter, etc.) are included.

Our analysis included the investigation of three of the most common types of TBIs, however, ideally, the vulnerability analysis of the human brain should consider all types of injuries. Maybe this could be the case in the future, as soon as tissue-level resistances become available corresponding to all injury types.

Our results are limited to the injury probability of humans seated in the driver's seat in the case of frontal crashes into a rigid barrier performed with 56 km/h impact velocity. However, since kinematic effects occurring on the head during crash tests were measured by test dummies – despite their excellent biofidelity – our results are influenced by differences in kinematic properties exist between humans and AATDs.

The applied tissue-level resistances were taken from the literature [21] and were used earlier during

the development of BrIC injury indice [23]. Previous research based on investigations of real-world crashes [14], [19] found that BrIC may overestimate the injury risk, thus there is a need for further research. The source of this overestimation is not known, however, if it derived from the applied resistance models or the FE simulation technique, it would influence our results as well.

Since the measured HIC_{15} values of the selected frontal crash tests belong to the 107-660 interval (Table 2), kinematic effects obtained by scaling the measured accelerations may be less reliable at a much larger HIC₁₅ intensity level. Primarily, it derives from the possibility, that the rotational and linear acceleration histories may have different characteristics and tendencies in the case of this larger HIC₁₅ intensity level. Therefore, the curve of the proposed modified risk curve (Fig. 8) is represented by dashed line in the $HIC_{15} > 1000$ interval, indicating that the results may be less reliable for these high HIC15 intensity cases which rarely occur during such tests. Accordingly, from a practical point of view, the lower tail of the curve (which is represented by solid line in Fig. 8) is much more important, since thresholds should be chosen from this interval which belongs to lower HIC₁₅ intensities and lower injury risks.

From a theoretical point of view, the tissue-level response of the human brain can highly depend on the impact velocity beside HIC_{15} values. Therefore, it is not completely valid to use the same $HIC_{15} - P_{AIS4+|HIC_{15}}$ curve for crash tests performed with different impact velocities. Accordingly, constructing further $HIC_{15} - P_{AIS4+|HIC_{15}}$ curves with different impact velocities could be an important task in the future.

The investigation of injury probability during different test types (e.g., side impacts instead of frontal crashes, dummies seated at different locations, different impact velocities, etc.) should be the topic of further research as well as the analysis of occurrence of injuries with different AIS levels.

5. Conclusions

Results of the tissue-level reliability analysis of the human brain indicate a considerably higher injury risk than it is predicted by current safety standards. Based on these results, a new risk curve which follows a lognormal distribution was proposed. Sensitivity analysis confirmed that rotational effects have a major contribution to the observed injury probabilities, which strengthens the common belief that rotational

effects are the primary cause of brain injuries. These observations suggest that the use of a solely translational acceleration based injury metric contains several uncertainties which can lead to relatively high injury probabilities even if relatively small translational effects occur.

Acknowledgement

This work was supported by the Higher Education Excellence Program of the Ministry of Human Capacities in the frame of Biotechnology research area of Budapest University of Technology and Economics (BME FIKP-BIO).

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