An Artificial Neural Network Predicts the Excessive Radiation Risk in Epidural Pulsed Radiofrequency (Eprf) Interventions - A Pilot Study

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Abstract

Objectives: Epidural pulsed radiofrequency (ePRF) interventions are successfully used in the treatment of patients with cervical, thoracic, and lumbar pain but they can be associated with high radiation doses. The scope of this study was to evaluate the ability of an artificial neural network (ANN) to predict preoperatively an excessive radiation risk in such procedures.

Materials and Methods: For 46 patients treated with ePRF, the dose area product (DAP) and procedure times were retrospectively analyzed. Additional patient, symptom, and surgical characteristics were collected based on the surgery protocols. An ANN was constructed to predict the excessive radiation as compared to the mean DAP value.

Results: Twenty-one patients were male (45.7%) and 25 females (54.3%). Mean values and ranges: age (61.76±2.2; 29-86 years), duration (26.65±1.43; 12-53 minutes), and DAP (694.63±113.83; 130.71-3,711.64 Gy/cm2). The resulted ANN contained 7 scaling neurons (inputs), 3 hidden neurons, and one probabilistic neuron (target). Important inputs for the acquired ANN were age, sex, diagnosis, side, and level of intervention. The experience of the surgeon and the duration of the surgery were not significant contributors in this ANN. The network exhibited a sensitivity of 1, a specificity of 0.43, an AUC (Area Under Curve, ROC chart) of 0.714.

Conclusion: It was possible to construct an ANN, which could predict if the radiation burden during an ePRF procedure would be higher than the average one. This could prove useful in optimizing the planning of ePRF procedures. Further studies with a larger series of patients are warranted.

Keywords: Artificial neural networks; Interventions; Prediction; Pulsed radiofrequency; Radiation risk.

Introduction

Pulsed radiofrequency (PRF) interventions are characterized as minimally invasive and target-selective procedures reducing the pain intensity in various chronic pain syndromes [1,2]. Many studies have demonstrated the effectiveness of this therapy [3-5]. Surgeons find it simple, easy and with a low risk profile [5,6]. Nevertheless, PRF surgeries are associated with specific risks too. The use of fluoroscopy can pose radiation risks not only for the patient but for the surgeon as well [7]. Health professionals working with ionizing radiation should always take into consideration the radiation dose they and their patients may receive during an interventional procedure and try, by using a careful preoperative planning, to eliminate or reduce the factors, which determine the level of these doses [8]. Artificial neural networks (ANNs), as computing systems inspired by biological neural networks, incorporate the technique of memorizing heterogeneous correlations between input and output patterns [9]. After a training phase, they can extrapolate to give answers to newly presented input data [9-11]. ANNs have been used since many years successfully for predicting outcomes in various medical fields [11-16]. Interestingly, up to this point, Neurromodulation scientists have conducted extremely limited research in this promising evolving domain [17-19]. The existing publications are based mostly on preclinical settings [20,21]. The scope of this pilot study was to generate initial observations on the feasibility of the ANN-technology to predict preoperatively an increased radiation risk in patients, who undergo ePRF interventions.
Materials and Methods

Patient population

A total number of 46 consecutive patients with chronic neuropathic pain (P) treated in our Department during the last 6 months with ePRF were enrolled (Table 1). The dose-area product (DAP) [22] and the procedure times were retrospectively analyzed. Additional patient (age, sex), symptom (low back-P, leg-P, back and leg-P, thoracic-P, cervical-P, left or right side), and surgical (experience of surgeons, level of intervention) characteristics were collected based on the surgery protocols. Most of the patients were female (54.3%), and the mean age was 61.76 years. The mean duration of the intervention was 26.65 minutes, and the mean DAP was 694.63Gycm². The most frequent symptom was the combination of low back- and leg-P (52.2%). Pain was manifested more often on the right side (43.5%). The PASHA catheter was placed in the majority of the cases at the conus medullaris level (93.5%). Surgeons with an experience of 2-5 years performed 56.5% of the surgeries.

Table 1: Patient, surgeon, and surgery characteristics.

| Variable                      | Value                                  |
|-------------------------------|----------------------------------------|
| Age (mean±SD; range) (years)  | 61.76±2.2; [29-86]                     |
| Sex                           |                                        |
| Male                          | 21(45.7%)                              |
| Female                        | 25(54.3%)                              |
| Diagnosis                     |                                        |
| Cervical-P                    | 2.20%                                  |
| Thoracic-P                    | 4.30%                                  |
| Leg-P                         | 6.50%                                  |
| Low back-P                    | 34.80%                                 |
| Leg-P & Low back-P            | 52.20%                                 |
| Side                          |                                        |
| Left                          | 28.30%                                 |
| Right                         | 43.30%                                 |
| Both                          | 28.30%                                 |
| Level of surgery              |                                        |
| Cervical                      | 2.20%                                  |
| Middle thoracic               | 4.30%                                  |
| Conus medullaris              | 93.50%                                 |
| Duration of the surgery (mean±SD; range) (minutes) | 26.65±1.43; [12-53] |
| DAP (mean±SD; range) (Gy cm²) | 694.63±113.83; [130.71-3,711.64] |
| DAP OVER MEAN                 |                                        |
| No                            | 78.40%                                 |
| Yes                           | 21.60%                                 |
| Surgeon experience            |                                        |
| <2 years                      | 23.90%                                 |
| 2-5 years                     | 56.50%                                 |
| >5 years                      | 19.60%                                 |

ePRF-Technique

The tip of the multifunctional PASHA-Catheter [23] (Figure 1) was placed in the epidural space by typical epidural puncture under fluoroscopy directly to the target root or at the level of conus medullaris. A motor stimulation at 2Hz was made followed by a sensory one at 75Hz, evoking a paresthesia in the painful area. When the expected response was observed, we applied the PRF for 4-12minutes (42 °C). The radiofrequency current was applied in short (20ms) and high-voltage bursts with a silent phase of 480ms, which allowed time for heat elimination. At the same time, we injected 40mg Dexamethasone (acis Arzneimittel GmbH, Gruenwald, Germany), and 6ml Ropivacaine 0.5% (AstraZeneca GmbH, Wedel, Germany).

ANN

An advanced analytics software (Neural Designer, Artificial Intelligence Techniques Ltd., Salamanca, Spain) was used to construct an ANN based on 7 input (age, sex, diagnosis, side, level of surgery, experience of surgeon, duration of the surgery) and 1 target (excessive radiation as compared to the mean DAP value from all patients, DAP OVER MEAN) variables. Nine patients were excluded from the analysis because of missing data. Variables from 21 patients were analyzed during the training phase (quasi-Newton training algorithm). The quasi-Newton method is based on Newton's method but does not require calculation of second derivatives. Instead, it computes an approximation of the inverse Hessian at each iteration of the algorithm, by only using gradient information [24]. Eight patients were included in the testing phase. The ANN was then used to predict the excessive radiation risk in 8 patients (validating phase).

Receiver operating characteristic (ROC) curve

The discrimination capacity of the ANN was tested with the ROC curve. A ROC curve is a graph, which plots in the x-axis the 1.0-specificity and in the y-axis the sensitivity calculated for every different threshold [25]. In order to calculate the points of the curve,
the threshold varies along the output probability of the testing instances in ascending order. In a perfect model, that can correctly classify all the instances, the ROC curve passes through the upper left corner, which is the point in which the sensitivity and specificity take the value 1. The closer to the upper left corner that the ROC curve passes, the better its discrimination capacity (the area under curve, AUC, for it would be 1) [26]. A random classifier, represented by the baseline, has an AUC of 0.5 [11].

Statistical analyses

All analyses (mean, standard deviation, range, ROC-curve, AUC) were conducted using SPSS, Version 17.0 (SPSS Inc., Chicago, IL, USA) and Neural Designer (Artificial Intelligence Techniques Ltd., Salamanca, Spain).

Results

Table 2: Inputs importance results for the artificial neural network (ANN).

| Variable           | Contribution |
|--------------------|--------------|
| Age                | 0.862        |
| Sex                | 0.861        |
| Diagnosis          | 0.86         |
| Side               | 0.86         |
| Level              | 0.86         |
| Surgeon experience | 0.859        |
| Duration of surgery| 0.655        |

The graphical representation of the network architecture is depicted in Figure 2. The resulted ANN contained 7 scaling neurons (inputs), 3 hidden neurons (representative of the complexity of the ANN) and one probabilistic neuron (target; DAP OVER MEAN = yes / no). Important inputs for the acquired ANN were age, sex, diagnosis, side, and level. Table 2 shows the importance of each input. The most important variable was Age, which got a contribution of 86.22% to the outputs. The experience of the surgeon and the duration of the surgery were not significant contributors in this ANN. The network exhibited a sensitivity of 1, a specificity of 0.43, an AUC of 0.714 (Figure 3), and a maximum gain score (maximum difference between the positive cumulative gain and the negative cumulative gain, i.e., the point where the percentage of positive instances found is maximized and the percentage of negative instances found is minimized) of 0.857 (in a perfect model = 1) (Figure 4). The calibration plot (Figure 5) showed a good calibration too.
Discussion

The goal of the study was to investigate the potential applicability of the ANN-technology in predicting an excessive radiation risk in ePRF patients. It is, to the best of our knowledge, the first identifiable article in the literature, which investigates the possible role of such constructs in improving the quality of surgeries in the epidural space. PRF represents a Neuromodulation therapy that is effective in the context of neuropathic pain [27]. It has emerged from an Austrian conference in 1995 [1,28], but the first procedure was performed on February 1st, 1996 [5]. It offers pain reduction without causing destructive lesions [29,30]. Although the mechanism of action has not been fully understood, laboratory experiments show real neurobiological processes modulating the pain signaling [3]. It has been used in treating various conditions, such as cervical [4,31,32] and lumbar radicular pain [4,31,33], sacroiliac and shoulder joint pain [34]. Table 3 presents some indicative studies investigating the efficacy of this modality [4,31-34]. Unfortunately, PRF requires fluoroscopy, which in turn is associated with exposure to hazardous ionizing radiation [35]. The DAP assesses the occupational dose and provides valuable information about the extent of the scatter dose and the appropriateness of the applied techniques [22]. It was first in 1992 that the Food and Drug Administration (FDA, USA) received some unverifiable reports linking the use of fluoroscopy to possible radiation injuries [36]. Since then, the issue of radiation exposure has been extensively addressed during different types of diagnostic procedures and surgeries, such as in lumbar discography [37-40], in vertebroplasty [39,40], in kyphoplasty [41], in minimally invasive transfemoral lumbar interbody fusion [42], and in pedicle screw insertion in the lumbar spine [43-45]. In pain practice, the radiation levels were explored during lumbar epidural steroid injections [38,46-52], in medial branch blocks and facet joint injections [38,50-54], in intercostal blocks [51], in stellate ganglion blocks [55], and in percutaneous adhesiolysis [51].

Table 3: Indicative publications on pulsed radiofrequency (PRF) [4,31-34].

| Author(s) (Reference) | Year | Condition | Outcome |
|-----------------------|------|-----------|---------|
| Vigneri et al. (33)   | 2014 | Lumbosacral radicular P | P reduction in NRS >2 points & >30% at 1 (53%) & 6 months (50%) |
| Chao et al. (31)      | 2008 | Cervical & lumbar radicular P | P relief in 55% & 45% of patients with cervical & lumbar P respectively after 3 months |
| Abejón et al. (32)    | 2007 | Lumbar radicular P | Decrease in NRS in patients with herniated disks but not in patients with FBSS after 3 months |
| Martin et al. (34)    | 2007 | Sacroiliac & shoulder joint P, radiculopathic P & sympathetically maintained P | P relief ranged from 5 to 19 months in different patient groups |
| Shabat et al. (4)     | 2006 | Cervical & lumbar P | P relief in 68% of patients more than 1 year |

FBSS: Failed Back Surgery Syndrome; NRS: Numeric Rating Scale; P: Pain

Potential biological effects following interventional procedures are manifested in the skin [36,56-58], in the eyes [58-60], in glands (thyroid, parotid) [58], and in several other tissues (breast, lung, bone, blood) [58,61-63]. In contrast to the above findings, the occupational exposure to X-rays seems unlikely to be associated with congenital abnormalities or childhood malignancies in the practitioners’ off springs [64]. An overview of the reported health risks due to radiation is provided in Table 4. Thus, proactively reducing the radiation risk is necessary to ensure the safety of surgeons, patients, and personnel as well [35,54,65]. The preprocedural planning should incorporate the evaluation of radiation risk to the patient considering all the relevant demographic, medical, and procedural risk factors [66]. Radiation reducing methods include, among others, minimization of beam-on time, minimization of the use of image intensifier magnification, proper collimation of the primary beam, additional beam filtration, lower dose-mode fluoroscopy, lower recording speed, higher X-ray tube potential, and image receptor as close to patient as possible [67]. Our study found that an increased radiation risk (DAP OVER MEAN) was noted in 21.6% of the surgeries, and this risk was correlated with age, sex, side, diagnosis, and level of surgery. Age was the most significant contributor. The existing literature provides no information about the role of age, sex, and side of surgery on the radiation exposure. The correlation of the exact pain cause (diagnosis) is also poorly studied. More data are accumulated about the level of surgery. For instance, Hwang et al. compared the radiation exposure during
Tissue Reactions

| Skin & hair       | Erythema, epilation, desquamation (dry & moist), dermal atrophy, ulceration, dermal necrosis, telangiectasia, hair loss (alopecia), squamous cell carcinomas |
|-------------------|--------------------------------------------------------------------------------------------------|
| Thyroid gland     | Thyroid cancer                                                                                   |
| Parotid gland     | Parotiditis, benign & malignant tumors                                                             |
| Eye               | Detectable opacities, visual impairment (cataract)                                                 |
| Breast            | Breast tumors                                                                                    |
| Lung              | Pneumonitis, pulmonary fibrosis                                                                   |
| Blood             |                                                                                                  |
| Bone              | Mature bone: bone marrow hypoplasia, fractures, dental caries Immature bone (children): growth arrest |

Only 19.6% of the surgeries were performed by a surgeon with an experience of >5 years and 23.9% by a surgeon with an experience of <2 years. The experience of the surgeon was not a significant contributor in our ANN, although the literature provides evidence that the interventionalist experience constitutes a major factor [54,68-71]. It has been documented that residents who perform spine surgeries receive more radiation in comparison to residents who perform other interventional procedures [68]. Fluoroscopy times and patient doses were found to be reduced in the presence of experienced physicians during cerebral and lower limb diagnostic procedures [69], and during endoscopic retrograde cholangiopancreatography (ERCP) [70]. In addition, the presence of a coach, who gave the pain physicians instructions to minimize their received scatter dose during 596 interventional pain procedures, achieved a significant dose reduction of 46.4% [54]. Another study of 402 endourological interventions showed that surgeons reduced their fluoroscopy times up to 55% after receiving information/advice about their fluoroscopy manners. This finding was valid only for experienced surgeons and for easy procedures [71]. In contrast to these studies comes a report on patients undergoing coronary artery angiography [72]. The experience of the cardiologists was not related to the patient received dose. In the proposed ANN, the duration of the surgery was not a significant contributor. Impressively, publications which investigate the role of the operative time could not be retrieved. Fluoroscopy time is mainly employed in most of the reports. For example, Chida et al. found a good correlation (r=0.801, p=0.0001) between radiation dose and fluoroscopic time for the radiofrequency catheter ablation procedures but not for the percutaneous coronary intervention procedures (r=0.628, p=0.0001) [73]. The ANNs as models, which employ a dynamic concept for interpreting outcomes and which are capable of adjusting their indigenous framework with respect to a functional target, incorporate criteria that are of importance individually, and as such could be more efficient in predicting outcomes than conventional regression models [11]. They have been used extensively in medicine. During the last years, many papers on ANNs in Neurosurgery have been also published. The networks were applied in terms of diagnosis, prognosis, outcome prediction, and biomechanical assessments [12]. Table 5 presents some indicative publications [11,13,18,19,74-78]. Interestingly, functional Neurosurgery is rarely represented [17-19]. For example, McCartney et al. collected online questionnaire responses from 607 patients with facial pain syndromes [18]. The authors designed an ANN to diagnose various facial syndromes (trigeminal neuralgia, nervus intermedius neuralgia, glossopharyngeal neuralgia, temporomandibular joint disorder, and atypical facial pain) with great accuracy. The first attempt to apply an ANN in the diagnosis of facial syndromes goes back to 2006. Limonadi et al. examined 100 patients with facial pain, who were asked to fill in a facial pain questionnaire [17]. After an interview, a formal diagnosis was assigned to each patient. The ANN was able to retrospectively predict the correct diagnosis for 95 of 100 patients (95%), and prospectively determine a correct diagnosis of trigeminal neuralgia Type 1 (sensitivity: 94%; specificity: 83%) in 43 new patients. The ability of the ANN to accurately predict a correct diagnosis for the remaining types of facial pain was limited by the sample size [17]. Furthermore, Hosen used an ANN to select the best features and to discriminate between essential and parkinsonian tremor using spectral analysis of tremor time-series recorded by accelerometry and surface EMG signal [19]. He reported an ANN-efficiency of 87.5% in both feature extraction and in pattern matching tasks in a complete classification system. Our model exhibited a sensitivity
of 1, a specificity of 0.43, and an accuracy of 0.714. Even though the reported accuracy is not optimal (in the authors’ opinion, due to the small sample size), our results support the further evaluation of the ANN-methodology in future research. The current pilot study has some constraints. To start with, the sample size is small and, thus, the training and validating groups contain a limited number of patients. Further studies with a larger series of patients are warranted. Secondly, the Body-Mass-Index (BMI) could not be retrieved from the patient records and incorporated in the ANN. This is important because it has been shown that, when increasing patient thickness, radiation doses are increased [79]. Smuck et al. recorded the fluoroscopy times for 202 patients and the total procedure times for 137 patients in whom spine injections were performed [52]. The authors found a 30% increase in the mean fluoroscopy time (p=0.032), and a 35% increase in mean procedure time (p=0.031) in the group of overweight patients. In addition, Hanu-Cernat et al. reported on 127 patients treated with fluoroscopically guided spinal procedures [53]. They confirmed a correlation between weight and DAP (r=0.23, p<0.05). In other studies, the weight of the patient had no significant influence on the received dose [54]. For example, Chida et al. studied 200 cardiac intervention procedures and found a poor correlation between body weight and radiation dose (r=0.434, p<0.05) [73]. The lack of an exact diagnosis in our population is also an important drawback. Many publications underline the correlation of the diagnosis with the received radiation. A prospective study conducted on 100 patients treated with TFESIs showed that the patients with lumbar spinal stenosis had a statistically significant higher exposure time (p=0.037) as compared to patients with a herniated nucleus pulposus [46]. Hanu-Cernat et al. reported that patients with spinal pathology had higher radiation exposure than those without (r=0.28, p<0.005) [53]. Although the ANN-methodology presents many advantages [10,11], it exhibits some disadvantages too [12]: (a) the determination of the optimal algorithms is empirical; (b) the extraction of explicit relationships between predictors and outcomes is difficult; (c) the propensity to overfit the model during the training phase is evident.

Table 5: Indicative publications on artificial neural networks (ANNs) in neurosurgery [11,13,18,19,74-78].

| Author(s) (Reference) | Year | Condition | Scope (D, P, O, BA) |
|-----------------------|------|-----------|-------------------|
| McCartney et al. (18) | 2014 | Facial pain syndromes | D: Correct diagnosis of patients with different facial pain syndromes |
| Hosen (19)            | 2013 | Tremor (Parkinsonian / essential) | D: Discrimination between Parkinsonian tremor and essential tremor |
| Matis et al. (11)     | 2016 | Lumbar disc herniation | P: Satisfaction derived from the hospital stay |
| Azimi et al. (74)     | 2014 | Lumbar spinal canal stenosis | P: Satisfaction derived from the surgery |
| Dumont et al. (75)    | 2011 | Aneurysmal SAH | P: Symptomatic cerebral vasospasm |
| Azimi et al. (76)     | 2014 | Childhood hydrocephalus | O: Predicting endoscopic third ventriculostomy success |
| Arle et al. (77)      | 1999 | Epilepsy | O: Predicting outcome in epilepsy surgery |
| Amaritsakul et al. (78) | 2013 | Spinal pedicle screws | BA: Optimal design of pedicle screws |
| Wang et al. (13)      | 2002 | Joint moments | BA: Representation of the relationship between EMG signals and joint moments |

Conclusion

The current study suggests that it is possible to construct with the aid of an advanced analytics tool an ANN, which can predict if the radiation burden during an ePRF procedure will be higher than the average one. Our findings have a practical relevance in the context of a better preoperative planning of ePRF interventions. The same concept could be applied in the investigation of the radiation exposure during spinal cord stimulation (SCS) surgeries or during intrathecal catheter tip placements.

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