EDITORIAL

Neurosurgical contributions of the Swiss surgeon, Rudolf Ulrich Krönlein—A further pioneer in Swiss neurosurgery

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Introduction

In an earlier contribution, the authors reported about the outstanding neurosurgical activities and publications of the Swiss surgeon and Nobel Prize laureate, Emil Theodor Kocher (1841–1917), with special emphasis on his perceptions in the fields of epilepsy and tumour surgery [12]. Furthermore, his methods in spinal surgery and his theories on raised intracranial pressure (ICP) were appreciated [9, 12].

Many Swiss surgeons have made important contributions to neurosurgery throughout history. However, few have made such important contributions as those of the Swissborn pioneer/surgeon, Rudolf Ulrich Krönlein (1847–1910). The aim of this article therefore is to introduce Krönlein's biographical information and scientific contributions to the neurosurgical society. Furthermore, the authors discuss similarities of the German-speaking surgical generation of this time and draw conclusions concerning our role in medical enterprises today.

Methods

A recapitulation of Krönlein's biographical information and outline of his relevant neurosurgical publications are derived from his articles cited in this essay. The literature research was strongly supported by the team of the antiquarian bookshop, Söhn (Marburg, Germany).

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Results

Biographical information

Krönlein was born in Stein am Rhein (Switzerland) on 18 February 1847. He went to secondary school in Schaffhausen and started his medical education at Zurich University in 1866 [33]. During the winter term in 1867, he carried out an internship with the anatomist Hermann von Meyer (1815-1892). In 1868, Krönlein attended Bonn University in Germany for a semester. In 1870, he successfully passed the state medical examination in Zurich. Krönlein earned his doctorate on the open treatment of wounds ("Die offene Wundbehandlung, nach Erfahrungen aus der chirurgischen Klinik zu Zürich") while working for the German surgeon Edmund Rose at Zurich University in 1870-1873 [16]. In serving as a military surgeon in 1870-1871 during the French-German war, Krönlein followed his teacher Rose to Berlin. Here, Krönlein worked at the military hospital Tempelhofer Feld, which was administrated by Rudolf Virchow (1821-1902). On the basis of Virchow's recommendation, Krönlein continued his residency as an assistant for Bernhard von Langenbeck (1810-1887), director of surgery at the University Clinic Charité in Berlin, Germany, in 1874. Beginning in the winter of 1878, Krönlein was asked to be the deputy head of the surgical clinic at Giessen University in Germany for a year. For this, he was appointed associate professor by the Hessian ministery. After his return to Berlin, Krönlein was asked to organise the reconstruction of the royal clinical centre (Ziegelstrasse, Berlin). In 1881, his mentor Rose was elected as head of the Bethanien Hospital in Berlin, and von Langenbeck supported Krönlein's appointment as professor and head of the surgical University Clinic in Zurich. He held this position for almost 30 years (1881-1910) (Fig. 1). His main surgical interests were:



surgery of the lung, appendix, stomach, thyroid gland, pancreas, pharynx and peritonitis. His influence on the development of a neurosurgical subspecialisation will be discussed in the next paragraphs. In 1910, Krönlein died as a consequence of angina pectoris.

Krönlein's contributions to the neurosurgical field

Krönlein's publication list comprises 84 articles, of which 19 deal with neurosurgical topics [13–33]. All of his articles are published exclusively in German.

1872 "Die offene Wundbehandlung, nach Erfahrungen aus der chirurgischen Klinik zu Zuerich" (The open treatment of wounds, based on experience from the surgical clinic in Zurich)

In his dissertation, Krönlein demonstrated early that he supported rational statistics in empirical research and modern medicine [16]. In the introduction of his dissertation, he emphasised the value of statistical analysis to test his hypotheses based on his observations in surgery as well as for the establishment of general principles in medicine. His work comprised numerous tables containing numbers of complications, survival times and detailed outcome reports on patients with limb amputations. Using statistical methods, he directly compared two treatment periods (1860-1867 and 1867-1871).



Fig. 1 A portrait of Rudolph Ulrich Krönlein



1882 "Klinischer Beitrag zur topischen Diagnostik der Hirnverletzungen und zur Trepanationsfrage" (Clinical contribution concerning topical diagnostics in traumatic brain injury and indications for trepanation)

In 1882, it became evident that Krönlein supported the modern theory of cerebral topography as proposed by Fritsch and Hitzig [7], Ferrier [6] and others. However, he stressed the difficulty of transferring the new knowledge about functional neuroanatomy to diagnostics in traumatic brain injury (TBI). Krönlein realised early that the pathologies following TBI are rarely circumscribed brain lesions. With a contemporary case report, Krönlein contributed to neurophysiology: He described the clinical course of a 26year-old worker with a right-sided impression fracture of the parietal bone and focal seizures of the left arm, followed by a postconvulsively intensified paresis (Todds' paresis). After successful resection of the impressed bone fragment, Krönlein reconfirmed the close connection between Rolando's cortical area and limb movements in humansan insight that had previously mostly been gained by animal experiments. Following this experience, Krönlein supported the consequent surgical treatment of impression fractures of the skull, in particular in connection with signs of elevated intracranial pressure (ICP) such as vomiting and bradycardia [20, 24].

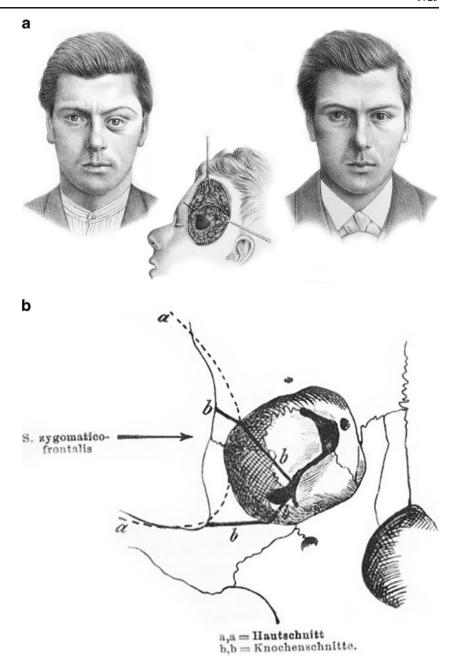
1886 "Ueber die Trepanation bei Blutungen aus der Art. meningea media bei geschlossener Schädelkapsel" (Concerning trepanation for haemorrhage of the middle meningeal artery with intact cranial bone)

Krönlein emphasised the high value of surgical treatment for epidural haematomas and called trepanation for this indication a life-saving measure [24]. Without additional diagnostic tests other than the clinical observation of the surgeon, he described the difficulty of choosing the right location for trepanation in patients without external signs of trauma. Krönlein discussed the issue of ICP and referred to the publications of Pagenstecher [35], von Bergmann [43–45] and Duret [5].

1888 "Zur Pathologie und operativen Behandlung der Dermoidcysten der Orbita" (Concerning the pathology and surgical treatment of dermoid cysts of the orbita)

In 1888, Krönlein described a 21-year-old farmer with a painless left-sided periorbital tumour and resulting bulbar asymmetry in a publication for the journal "Beiträge zur klinischen Chirurgie" (Fig. 2a) [31]. For osteoplastic resection, he developed the lateral orbitotomy (Fig. 2b). The histopathological workup revealed a dermoid cyst. By this action, Krönlein became one of the pioneers of orbital decompression, later commonly used for Graves' ophthalmopathy surgery [1].

Fig. 2 a Krönlein's patient, who underwent resection of a dermoid cyst via lateral orbitotomy pre-, intra- and postoperatively. b Krönlein's description of the skin incision (a, a) and osseous exposure (b, b) (from [31])



1891 "Ueber den gegenwärtigen Stand der Hirnchirurgie" (About the recent state of brain surgery)

On 25 October 1890, Krönlein lectured to the Central Medical Assembly (Aerztlicher Centralverein) on the relevance of the surgical treatment of epilepsy [22]. He underlined the importance of epilepsy surgery in patients with impression fractures of the skull and posttraumatic cortical scars. He reported that localised cortical resections for removal of "epileptogenic centres" as proposed by Horsley were technically feasible. Krönlein elaborated the clinical difference of elevated ICP in slowly growing intracranial lesions in contrast to the acutely raised ICP as in intracranial haematomas after

traumatic brain injury. He then discussed the operative treatment modalities for hydrocephalus, especially concerning the ventricular puncture. In his lecture, he advised against surgical interventions in patients with severe psychiatric disorders.

In his lecture, Krönlein furthermore reported his experiences in the surgical treatment of open head trauma. From 1881 to 1890, 19 patients with this kind of trauma were treated in his clinic. Four of nine patients with bullet wounds died; six of ten patients survived surgery for an impression fracture of the skull using the aseptic technique. He then discussed the pathology and the surgical strategies for



intracranial abscesses, also referring to the expertise of his colleagues. After that, Krönlein mentioned the epidemiology and operability of brain tumours. His report was based on the available literature. Until his lecture, 22 trepanations had been reported [22]. Seven trepanations were unsuccessful (lesion not found, surgery aborted), and four patients died as a consequence of the failed intervention. Of the remaining 15 patients, 6 died from the surgery. Only eight patients were cured, but at the expense of neurological deficits. Krönlein concurred with von Bergmann's opinion that surgery for brain tumours should be reserved for a small portion of patients. In July 1895, Krönlein performed his first trepanation in Zurich for an intracranial mass lesion.

1892 "Ueber Schädelbrüche" (About skull fractures)

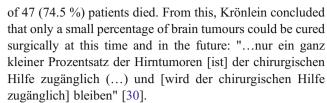
Krönlein motivated the fellow physician Anna Heer from Zurich to do her inaugural dissertation on skull fractures [11]. Heer described the specific post-mortem pathoanatomic findings in 29 persons with skull-base fractures. These findings were correlated to the clinical course of the respective person, the associated neuronal injury and experimental observations in the literature. In her dissertation, Heer proposed a modern classification of skull-base fractures.

1895 "Zur retrobuccalen Methode der Freilegung des 3. Astes des N. trigeminus" (About the retrobuccal method for exposure of the third branch of the trigeminal nerve)

In 1895, Krönlein described the successful extracranial neurectomy of the inframaxillar nerve in the region between the mandibular lingua and the skull base in two patients with trigeminal neuralgia using ether anaesthesia [32]. Both patients were pain free after the intervention. In one of the presented cases he described the technique of furling the nerve using a clamp. According to his observation, this technique led to an "evulsion" of the peripheral trigeminal branch over a 13-cm length up to the Gasserian ganglion. In his publication Krönlein not only discussed potential risks and benefits of his own and other extracranial approaches, but also those of intracranial methods used by other authors. The practical realisation of his own method was preceded by theoretic-anatomical considerations verified in the dissecting room (Fig. 3) [27, 32].

1895 "Zur operativen Chirurgie der Hirngeschwülste" (About surgery of brain tumours)

In 1895, Krönlein described how the number of brain tumour extirpations described in the international literature had increased from 15 (before 1890) up to 67 patients in 1894 [14, 30]. According to him, 20 of the 67 (29.6 %) patients died after brain tumour surgery [30]. In a different literature-based collective with attempted but impossible (e.g. tumour not found) or incomplete tumour resection, 35



Krönlein mentioned the 50 % mortality of surgical treatment of intracerebral tuberculomas. Furthermore, he stated that this type of lesion was the most frequent intracranial lesion. He added a further report of intracerebral tuberculoma himself: beginning in February 1895 he reported on a 43-year-old patient who developed right-sided brachiofacial focally initiated grand-mal seizures. Krönlein suspected the lesion to be localised in the hand and facial region of the left-sided motor cortex. A tuberculoma was suspected because the patient's father and sister suffered from tuberculosis. Krönlein performed an osteoplastic trepanation according to the technique of Wagner [50] (Fig. 4). He localised the left-sided area of Rolando according to the recommendations of Bennett and Godlee [30]. After opening the dura, eight tuberculomas were identified and removed. The operation under ether anaesthesia took one hour. Postoperatively, the patient suffered from severe brachio-facial hemiparesis and dysarthria, which improved over the following months. Histopathological workup confirmed the diagnosis of tuberculosis. Because of recurrent epileptic seizures, the patient received a second surgical intervention for a suspected local relapse in November 1897. However, intraoperatively only postoperative cortical scarring was found [14].

In May 1905, Krönlein again reported about this patient to the Central Medical Assembly (Aerztlicher Centralverein) in Zurich. At this point, a slight arm paresis persisted in the patient. The gait was unaffected, the tuberculosis was cured, and the epileptic seizures had ceased [18].

1895 "Weitere Bemerkungen über die Lokalisation der Hämatome der Art. meningea und deren operative Behandlung" (Further comments on the localisation of haematomas from the middle meningeal artery and their surgical treatment)

Krönlein devoted himself to the differential topography of epidural haematomas (anterior, middle and posterior) in this article [28]. He described the diagnosis and surgical treatment (trepanation) of a 47-year-old patient who suffered from middle menigeal arterial rupture after a heavy fall. After the patient died from the severe injury, an autopsy revealed infratentorial extension of the haematoma (Fig. 5). For situations with preoperatively suspected infratentorial extension of the mass lesion, Krönlein recommended the retromastoidal trepanation. In this work, he extensively discussed the value of tamponade or ligature of the ruptured arterial vessel.



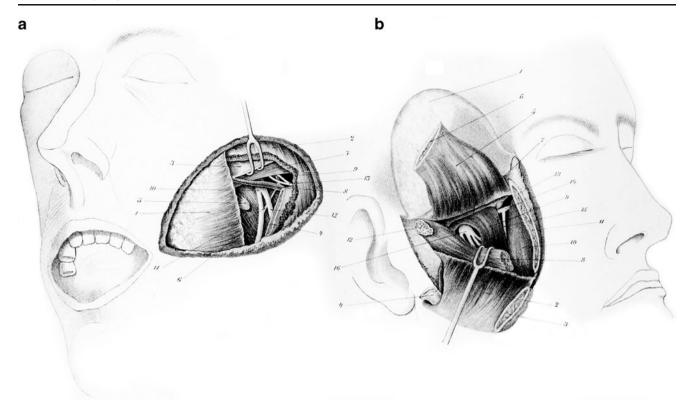


Fig. 3 Krönlein's sketch of surgical exposure of the third trigeminal nerve branch at the ovale foramen (labelled no. 16 in the figure) (from [27])

The same issue of "Beiträge zur klinischen Chirurgie" included an article by his co-worker, R. Gubler, based on Krönlein's ideas [10]. Gubler here addressed patients with complicated skull fractures, which he subdivided into a group with open skull fractures (without primary complications) and a group displaying the combination of skull



Fig. 4 Postoperative photography of the patient who underwent surgical resection of a cortical tuberculoma (from [30])

fracture and additional injury of the dura and/or blood vessels. From his perspective, "open" meant laceration of the skin in contrast to solely subcutaneous damage of the bone or deeper layers. Patients with impression fractures who received surgery at a later time displayed a worse clinical course than those who were operated on immediately. All patients with laceration of a dural sinus died from their injury; patients with head trauma and accompanying rupture of the middle menigeal artery displayed a mortality rate of 62 % despite surgery.

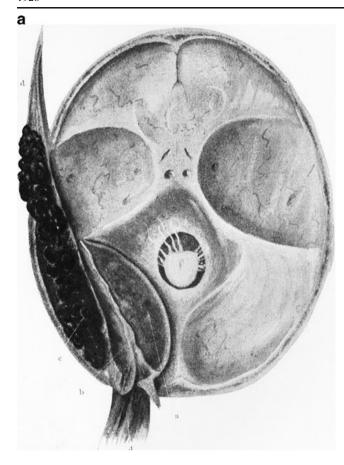
1898 "Zur cranio-cerebralen Topographie" (Concerning the cranio-cerebral topography)

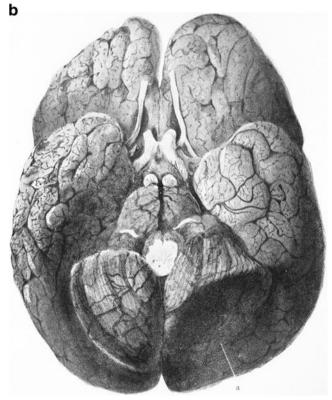
In his publication concerning the cranio-cerebral topography, Krönlein developed the construction of a craniometer (see also the following paragraph) [29]. His report was based on the constant relations between the cortex and skull, as demonstrated in the anatomical atlas by Froriep [8].

1899 "Ein einfaches Kraniometer" (A simple craniometer)

In the journal "Centralblatt für Chirurgie", Krönlein described his simple craniometer ("einfachen Kraniometer") (Fig. 6), whose construction was based on information generated in his previous works [17, 29]. The possible craniocerebral localisations were based on relative metrics that were proportional to each other [17]. The following points







▼Fig. 5 In 1895, Krönlein described an infra- and supratentorial epidural haematoma in a patient with traumatic brain injury. a The letters "a" and "b" indicate the sinus and dura with the haematoma that have been detached from the bone; "c" indicates the epidural haematoma, "d" the dural remnants. b "a" and "b" indicate a cerebellar hemisphere that is compressed by the haematoma (from [28])

and structures could easily be detected by using the craniometer: the division and end of the sylvian fissure, the upper and lower end of the central sulcus, both of Krönlein's trepanation points for the approach for haematomas of the medial meningeal artery and the location for trepanation of temporal otitic abscesses as described by von Bergmann [17]. The craniometer was made from six metal clasps and could be purchased from the instrument draftsmen Hanhart & Ziegler in Zurich.

1899 "Beitrag zur Lehre der Schädel-Hirnschüsse aus unmittelbarer Nähe mittelst des Schweizer Repetier-Gewehrs Mod. 1889" (Article on close proximity bullet wounds from the Swiss repeating rifle model 1889)

Krönlein reported on four suicide fatalities and one attempted suicide who used the 1889 model of the Swiss repeating rifle (calibre: 7.5 mm; bullet weight: 13.8 g; bullet composed of nickel-plated cap, initial speed: 600 m/s) [13]. In this article, he pointed out a distinctive feature: in a 32-year-old suicide victim he found scattering of the empty cranial cavity. The cerebrum and cerebellum were found lying next to the dead person; the brain had been separated from the spinal cord at the height of the medulla oblongata. A bullet channel, however, could not be determined. Further cases were published 2 years later [25]. Still today, the mechanism of evisceration of the brain without a bullet channel after a so-called "Krönlein shot" is discussed [36].

1900 "Chirurgie des Kopfes", **1.Auflage** (Surgery of the head, 1st edition)

In 1900, von Bergmann, von Bruns and von Mikulicz released the three-volume "Handbuch der praktischen Chirurgie" (Compendium of practical surgery) [49]. In the first volume, surgery of the head was explained in 1,120 pages. Ernst von Bergmann (1836-1907), who succeeded Krönlein's teacher, von Langenbeck, as head of the surgical university clinic in Berlin in 1882, had become one of the first German pioneers in neurosurgery (Fig. 7) [41–48]. Together with von Bergmann and two of his co-workers in Zurich (Schlatter and Wiesmann), Krönlein composed the book chapter "Verletzungen und Krankheiten des Gehirns, seiner Hüllen und Gefässe" (Trauma of the brain, its covering and vessels) in the second

Fig. 6 Krönlein's craniometer for the localisation of the central sulcus ▶ (b) and the sylvian fissure (c) was based on anatomical studies (a) (from [17])



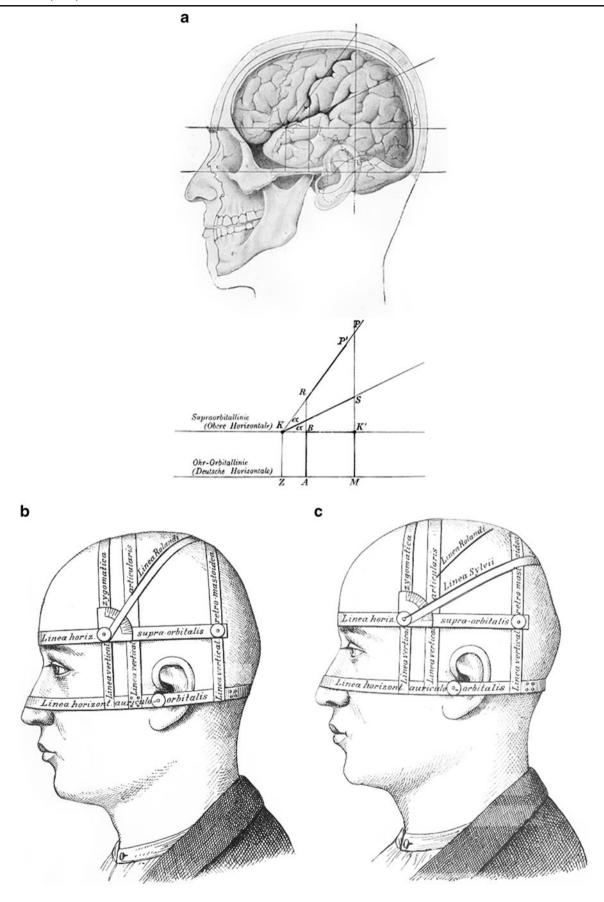






Fig. 7 Ernst von Bergmann is shown immediately before starting a trepanation at the Charité in Berlin

section of the compendium. Table 2 displays the chapter titles of the 4th edition of the compendium.

Already in 1885, Krönlein had motivated his coworker Wiesmann to report on the "modern" surgical treatment of TBI in Zurich, based on a case series of 123 patients [51]. In his article, Wiesmann discussed the clinical course of TBI patients from the Zurich Surgical Clinic (1803-1883) and from the literature, as well as the indications, techniques and value of trepanation in

various forms of traumatic intracranial haemorrhage and impression fractures. In the majority of Wiesmann's cases, an epidural haematoma was found following the trauma. Encouraged by his teacher Krönlein, Wiesmann was the first German-speaking physician to directly compare and statistically analyse the effects of trepanation or conservative treatment in a large case series. A total of 42 patients (34.1 %) received trepanation (with optional direct ligature of the medial meningeal artery). In five cases (4.0 %), surgery for an impression fracture was performed. Twenty patients (16.3 %) were only observed by the physicians, while in 56 injured patients (45.5 %), the best supportive therapy with antiphlogistic measures, phlobotomies, or application of cooling or laxatives was implemented. In summary, a total mortality of 64 % was observed with a distinct difference in mortality depending on the treatment: the mortality of the surgically treated group was 28 % in contrast to 90 % in the conservatively treated group. Of the surviving 36 %, 33 % recovered well and 3 % showed persisting neurological deficits. In his article, Wiesmann emphasised the danger of epidural haematoma in nonoperated patients [51].

1901 "Totale Oberkieferresektion und Inhalationsnar-kose" (Total maxillary resection and inhalation anaesthesia)

Table 1 Krönlein's brain tumour patients from Zurich, 1895-1904, from [39]

Age (gender)	Symptoms	Surgery/date	Histopathology	Clinical course
43 years (m)	Focally introduced generalised seizures	Left frontoparietal trepanation, resection of cortical lesion (July 1895)	Tuberculoma	Transient postoperative aphasia, persisting right-sided upper limb paresis, no recurrence of seizures during the 9-year follow-up
52 years (m)	Right-sided march of convulsion, Todds' paresis, headache	Left frontoparietal trepanation, resection of cortical lesion (April 1903)	Tuberculoma	Right-sided hemiplegia, died 9 months postoperatively
61 years (m)	Left-sided march of convulsions, headache	Right frontoparietal trepanation, stimulation of the cortex with electrical current, no lesion found intraoperatively (19 July 1899)	Autopsy revealed bi- hemispheric sarcoma	Died 3 February 1901
44 years (m)	Right-sided hemiparesis, focal seizures	-	Autopsy revealed left- hemispehric sarcoma	Died 1903
25 years (m)	Papilloedema, focally introduced generalised seizures, left-sided hemipare- sis	-	Autopsy revealed right- hemispheric glioma	Died 1900 after epileptic seizure
27 years (f)	Right-sided hemiparesis, headache	-	Autopsy revealed left- sided intraventricular sarcoma	Died 1903
40 years (m)	Papilloedema, ataxia	-	Autopsy revealed right- hemispheric cerebellar tuberculoma	Died 1904



Table 2 Topics treated by the authors of the compendium "Chirurgie des Kopfes", 4.Auflage, 1913 (Surgery of the head, 4th edition) (translated by the authors) [40]

- Congenital surgical diseases
- Cerebral concussion
- Intracranial pressure and surgery for elevated intracranial pressure
- Injury of intracranial blood vessels
- Injury of the cranial nerves within the skull and at the skull openings
- Contusions and wounds of the brain
- Traumatic meningitis
- Brain efflux and swelling
- Brain abscesses
- Thrombosis of the intracranial blood vessels
- Epilepsy and their surgical treatment
- Mental illnesses after head trauma and surgical therapy of mental illnesses
- Surgical therapy of brain tumours
- Pituitary surgery
- Techniques for trepanation, CSF puncture, resection of the skull bones, craniotomy, craniectomy, osteoplastic closure and duraplasty

Krönlein repeatedly discussed total maxillary resection in cases of facial bone tumours [21, 23]. In his article from 1901, he compared the surgical success before and after the implementation of aseptic methods (using the year 1870 as cutoff). Analysing the results of different surgeons, he described a mortality rate of 32 % before and 22 % after the use of aseptic methods as well as ether-based and chloroform-based anaesthesia. Krönlein finally lowered the mortality rate in his own series to 3 % by reducing the depth and length of anaesthesia. By these means, he was able to maintain the gag reflex in his patients, who had previously often suffered from severe aspiration-induced complications.

1906 "Hirnchirurgische Mitteilungen" (Messages in brain surgery)

In this article, Krönlein indicated the imminent danger of traumatic intracranial haemorrhages and the impact of the surgical treatment for this indication [19]. He reported that patients with severe head trauma were frequently observed in his clinic. Above, we mentioned his publication about trepanation in patients with epidural haematomas; in this article Krönlein defined subdural haematoma as a distinct entity. As an example of this, he described the case of a 27-year-old male who suffered from TBI with loss of conscience and focal epileptic seizures. From the semiology the physicians concluded the correct location of the intracranial lesion. After the subsequent trepanation an acute subdural haematoma could be treated successfully. Krönlein suspected a circumscribed

cortical contusion with moderate bleeding from the pial vessels as the cause of the subdural haematoma.

His article furthermore indicated that surgery for cerebral gliomas was already routinely performed at the Zurich University Clinic at the turn of nineteenth to twentieth century [19]. Krönlein referenced his co-worker Rütschi, who had reported about three surgically treated patients with intracranial tumours between 1895 and 1904, in his dissertation (Table 1) [39]. Krönlein himself described the case of a 30-year-old female with focal seizures and secondary generalisation in his article. After analysis of the semiology and using his craniometer, Krönlein had performed a craniotomy as described by Wagner in this patient, and was able to localise and resect a left frontodorsal subcortical tumour. Postoperatively, the right-sided hemiparesis and aphasia recovered significantly within weeks, and the seizures ceased. After 10 months the tumour relapsed. Pathohistological analysis by von Monakov revealed a malignant glioma. Krönlein emphasised the aspect of infiltration by brain tumours and named the tumour a "glioma malignum".

1913 "Chirurgie des Kopfes", 4. Auflage (Surgery of the head, 4th edition)

In the first volume of the 4th edition of the compendium of practical surgery (in the meantime five volumes, editors: von Bruns, Carré, Küttner, 4th edition, 1913), von Bergman and Küttner described surgery of the skull and soft tissue of the head in 165 pages in the first section. A second section was provided by von Bergmann, Krönlein and Küttner with detailed reports on special surgical topics concerning the brain, its coverings and blood vessels in 212 pages [40]. Table 2 depicts the chapters of the 4th edition that were written by the above-mentioned author collective. Krönlein's contribution, "die Ouetschungen und Verwundungen des Gehirns" (Contusions and wounds of the brain), was published in the compendium 3 years after his death. It is believed, that his part was updated by the co-author Küttner. Krönlein's observations regarding brain contusions were based on his own experiences and observations made during autopsies, as well as extensive histological findings. This enabled him to comment on the pathomechanisms of primary and secondary brain injury, the clinical courses and late sequelae (epilepsy, brain-organic psychosyndrome). In detail, he described the neurological signs found in localised brain lesions (cerebrum, cerebellum, basal ganglia, brain stem). In the acutely injured patient, Krönlein saw two indications for surgical intervention: removal of foreign bodies and prevention of septic infections. In the subacute stage, he suggested surgery for decompression of a swollen brain and for treatment of cerebrospinal fluid (CSF) fistulas.

In a further section of the book, Krönlein described the techniques for trepanation, CSF puncture, resection of the



skull bones, craniotomy, craniectomy, osteoplastic closure and duraplasty. As already developed by Kocher [12], Krönlein's craniometer was an early example of cranial navigation (Fig. 6).

Discussion

The Swiss surgeon Rudolf Ulrich Krönlein was part of a group of elite surgeons of his time [9, 12] who were not restricted by national boundaries in their education and practical work. Even though his neurosurgical contributions were only published in German, his works are still referred to in journals of today. As such, Altay et al. recently mentioned his original description of lateral orbitotomy [2].

During his medical studies, Krönlein had a semester in Bonn, Germany. Later, he was elected deputy head of the surgical clinic at Giessen University (founded in 1607) until his return to Switzerland for his final location at the Zurich Clinic for Surgery.

The path to Europe had already attracted Swiss intellectuals of these times, as mentioned by Bandelier recently [3]. In the field of medicine, another remarkable example is Albrecht von Haller (1708-1777). Between 1736 and 1753, he worked as a professor of anatomy, botany and surgery in Göttingen, Germany, where he contributed substantially to the upswing of the young university. Not only for political reasons, Switzerland was considered an attractive option for German physicians and scientists at the turn of the nineteenth century. Between 1834 and 1855, 40 % of the professors at Berne University were Germans—about the same number as from the canton Berne itself [38]. The German Wilhelm Conrad Röntgen (1845-1923) took his doctoral degree in Zurich on 22 June 1869. In 1879, he obtained his professorship at Giessen University, Germany, after having received his habilitation at Strasbourg in 1874 (at that time, Strasbourg belonged to Germany). As professor of experimental physics, he discovered the "X-Strahlen" (x-rays) at Würzburg University, Germany, in 1895 [37], for which he was honoured with the Nobel Prize in Physics in 1901.

The transnational intellectual exchange between the universities in Europe despite national boundaries, the impact of the industrial revolution, medical-technical progress (e.g. asepsis, anaesthesia, x-rays) and the entry of scientific methods into medical research with the emergence of the European "Forschungsuniversitäten" (research universities) allowed surgical pioneers of that time to develop and/or contribute to modern medicine. Like others (Kocher, von Bergmann, Vincent, de Martel, Chipault, Horsley and others), Krönlein represents a surgeon of a time of transformation in European medicine that influenced the birth of medical and surgical subspecialisations, such as neurosurgery. For Krönlein, the era of neurosurgery began at the end

of the nineteenth century, from which time on he was intensively concerned with brain surgery [13–33]. Other European and global surgeons also contributed to this eventful time: Kocher (1841-1917), von Bergmann (1836-1907), Vincent (1879-1947), de Martel (1875-1940), Chipault (1866-1920), Cushing (1869-1939), Durante (1844-1934) and Horsley (1857-1916). This period was markedly distinct from the latest regimentations in medical enterprises today.

The times of the neurosurgical pioneers with an impact on the genesis of this subspecialisation in the nineteenth century were often hallmarked by a tight connection with the European model of the "Forschungsuniversität". Those research universities could afford regulated and expensive laboratories, which also facilitated Cushing's experiments during his year of travel [4, 12]. At that time, not only the publication activity defined the scientific ranking of the respective physician. Reputations had to be built up in an increasingly personal exchange between the surgeons and were not influenced by political preconditions—unlike in the 20th century [34]. This also explains the high transnational mobility of Krönlein and his colleagues.

The dominance of the German "Forschungsuniversitäten" in the nineteenth century, initiated by Humboldt, makes it easy to comprehend why German-speaking surgeons were highly involved in the early development of neurosurgical specialisations. They could express their innovative ideas much earlier than their colleagues from countries that established official governmentally funded research facilities at a later point in time.

The collectively high international mobility, the rather low political influence on their autonomic acting at that time, the acknowledgement of science-orientated medicine, the brave willingness to communicate their surgical experience in the margins of actual knowledge, the will for teamwork and the ability to be innovative conferred a special, unforgettable status to the surgical pioneers. These actors functioned as connectors between an irrational and speculation-based medicine on the one hand and modern medicine on the other hand. For us actors of the present, we have to conclude that creative leeway for us and our own productive dynamics in medicine will only be preserved if we manage to maintain flexibility, the prerequisites of which have been described above.

Conflicts of interest None.

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