Introduction

From the end of the 90s, several advantages of Ultrasound Guided Regional Anesthesia (USGRA) compared to classical techniques have been described\(^1\),\(^2\),\(^3\). Up to this moment, peripheral nerves or groups of nerves (plexuses) have been located either by anatomical landmarks and provoking nerve paresthesia or by electric nerve stimulation, inducing a motoric or sensory response. This led to a high rate of unsuccessful blocks, insufficient analgesia and probably to a high rate of unnoticed intraneural injections. Historically described and used techniques like fascial “clicks” by using blunt needles, provoking paresthesia by nerve needle encounters, injecting „ice-cold“ saline or the transarterial approach for axillary plexus, could cause discomfort or harm. The use of nerve stimulation to provoke a motoric nerve response had painful side effects when used in a fractured limb. The use of ultrasound for the first time allowed visualization of anatomy at the bedside. Technical improvements like smaller bedside ultrasound machines, higher frequency probes and better software solutions have led to a growing popularity of ultrasound guided nerve and fascial blocks worldwide. Further technical solutions, availability of affordable ultrasound machines all over the world and changes in clinical approach are necessary to improve patient safety\(^4\).

Material and Methods

Literature research of PubMed/ MEDLINE, Google Scholar and NYSORA learning system (nysoralms.com). Key words / search terms: Ultrasound guided regional anesthesia, nerve blocks,
facial blocks, efficacy and success rate of ultrasound guided nerve blocks, education and training in ultrasound guided regional anesthesia, needle guidance, needle tip detection and technical solutions, in plane and out of plane needle insertion, equipment, ultrasound machines, nerve injury, incidence of nerve injuries related to regional anesthesia, local anesthetic systemic toxicity (LAST), dual guidance, nerve stimulation, injection pressure monitoring, triple guidance, hygiene in regional anesthesia, infection prevention in regional anesthesia, regional anesthesia and coagulation disorders, patient safety in regional anesthesia. We included scientific reviews and meta-analyses, randomized controlled trials, prospective cohort studies, retrospective cohort studies, animal studies, cadaver studies, textbook chapters, case series, case reports, editorials and pertinent correspondence in English language, German language and French language in our research, to identify and address controversies and open questions related to USGRA. We did not perform Jada or GRADE scoring of the references. We did not perform meta-analysis. Thus, effect size and risk differences for the questions raised are not numbered. Aiming at an educational compilation and presentation of the current knowledge, we focused on the last 15 years, but also included very pertinent or groundbreaking older references. We analyzed all sources for relevance for the questions asked. The characteristics, quality and limitations of references are mentioned and discussed in the text, where deemed necessary.

**Indisputable advantages of direct imaging**

Ultrasound offers the real time imaging of three important aspects:

– Visualization of the anatomy. This includes the structures to block (plexus, bigger nerves of the upper and lower limb, fascial planes), but also surrounding tissue layers and structures to avoid like vessels or pleura. An important advantage is the fact, that ultrasound detects anatomical variations and abnormalities. For example, the relationship between nerves and vessels is very variable and with landmark techniques this may lead to failed blocks or to injuries.

– Visualization and guidance of the needle to avoid damage of anatomical structures on its pathway. This reduces the risk of needle trauma, though it can be challenging to visualize the needle tip at all times. This will be discussed later on.

– Ability to see the distribution and spread of local anesthetics in real time. If the applied volume doesn’t spread around the desired areas, the needle tip can and must be repositioned and adjusted. This was impossible with all the former techniques.

**Sonoanatomy:**

*Is it possible to get the whole picture?*

The ultrasound image must show at the same time the anatomical target structure and the needle tip. It is important to keep in mind that the image is two-dimensional, while anatomy is not. So profound knowledge of anatomy is necessary („you see what you are looking for“), but also practical training and knowledge about the technical features of the ultrasound machine. These skills are necessary to provide equivalent success compared to general anesthesia. Optimizing the image and understanding sonoanatomy requires knowledge of the underlying basic principles of physics like choosing the right probe, frequency selection, image depth, the use of time gain compensation, adjusting focus, using filters etc. Axial and lateral resolution of the image, as well as the depth of tissue penetration by the ultrasound beam, are influenced by frequency, pulse length and the position of the narrowest zone of the ultrasound beam, the so-called focus. In real time pictures of moving objects – like needles advancing in tissue layers – temporal resolution, i.e., the frame rate with which consecutive images can be generated, is also important. Modern ultrasound machines offer several presets, the use of which in turn requires profound anatomical knowledge of the structures one wants to see, block or avoid. Trainable skills include optimizing the angle of insonation by tilting, sliding, rotating, aligning the transducer to the anatomical target structures and varying the degree of pressure applied to the probe. The mnemonic “PART – pressure, alignment rotation, tilting” is useful and recommended in the literature. Providers should master the use of different Doppler-modi to identify vessels
and differentiate them from neural structures. M-Mode are useful to identify moving structures like pleura sliding or bowel movement, when performing fascial plane blocks at the trunk.

Knowledge of important acoustic artifacts like mirror artifact, reverberation artifact, acoustic shadows (by bone or air), acoustic enhancement (by fluids), noise and twinkling artifacts, lateral cystic shadowing etc. is of the most importance, as those phenomena may fake or occult anatomical structures and lead to incorrect needle guidance5,6,7. The needle itself may be reflecting the ultrasound waves so extensively, that it creates reverberation and mirror artifacts. A summary of different artifacts, their physical origin and significance, as well as of challenges presented by patients’ anatomy is presented at8.

How can we optimize training and education?

Structured training and education in ultrasound guided regional anesthesia should be mandatory for residents. In any training program it seems important that teachers emphasize basic, but helpful details like an ergonomic position of the ultrasound machine. A mandatory minimum number of ultrasound-guided blocks during residency is part of the specialist training program in several countries and teaching curricula have been implemented9 or fellowships suggested10. Remarkably, even very short training rotations of 4 weeks with structured instructions improved residents’ recognition of relevant sonoanatomy significantly11.

Some authors argue that competency-based education with skilled and dedicated supervisors, quality assessment, educational feedback and a structured educational environment is at least as important as the numbers performed, especially when it comes to difficult cases12. The exact amount of training needed is scientifically unknown, although there is some data from cadaver studies13, and is variably dependent on the trainees’ and trainers’ personal and didactic skills14. There are several training programs including cadaver workshops15,16 or meat models17 without one method being defined as “gold standard” based on scientific data and further research needed18,19. A combination of different methods like simulation, using meat models, debriefing, supervision and feedback recommended20. Reviews confirm that simulation in regional anesthesia training is useful21,22,23. Structured expert feedback is superior to self-directed learning on simulation training24. ESAIC recently published a guideline (PERSEUS regional anesthesia) with a strong focus on education, training and certification. They define an “expert trainer in ultrasound-guided regional anesthesia” and suggest performance indicators. To follow these guidelines will require profound change of national training programs, as they mostly still focus on numbers only and USGRA fellowships need to be established25. Software programs integrating pictures of the „real“ anatomy into the software of ultrasound machines may help to improve teaching and learning. Recent technical developments to guide needle placement close to the nerves without puncturing them, include passive magnetic ultrasound needle guidance technology, which improved accuracy of needle procedures in one study26 but is not yet widely available. Other possible technical improvements for teaching in the future include ultrasound combined with pressure guidance, video visualization guidance, electromyography guidance, electromagnetic Guidance Positioning Systems (GPS), image fusion guidance and the combination of artificial intelligence (AI) with neural networks and pattern recognition with ultrasound27. AI significantly improves recognition of anatomical structures by non-experts28 but its value in teaching and clinical setting is yet to be investigated29. Today there is no strong evidence of superiority for any of these to recommend them as a standard in teaching30. There is an ongoing debate how many different blocks the average anesthetist should master. Turbitt et al. raise the question if we really need more blocks or rather better practice and widespread implementation of some „basic blocks“, also called „high value nerve blocks“31. As ultrasound allows the development of more and more different approaches, this is an important question for further educational programs with regard to competency in basic regional anesthesia for as many anesthesiologists as possible. It is unclear how many different blocks need to be implemented in the standard of care and multimodal analgesia programs and thus in the mandatory education of specialists. It seems more promising to focus on blocks that have been proved effective, efficient and easy to implement in any clinical setting19,31,32,33.
Is an in plane needle insertion really safer than out of plane?

In the author’s personal experience it is crucial, that beginners understand the terms „short axis and long axis“, which refer to the anatomic structure, and the terms „in plane and out of plane“ that refer to the position of needle and probe. In plane signifies the needle parallel to, out of plane perpendicular to the long axis of the probe.

There is no data to establish a superiority of one of these methods with regard to patient safety. A topic of controversy is the approach to the interscalene block. Dorsal scapular and long thoracic nerves are often difficult to visualize inside the medial scalene muscle. They are prone to injury by an in plane needle path through the muscle\(^{34}\). A direct comparison of both techniques in an RCT on 84 patients with interscalene catheters did not find any difference in complications or success rate\(^{35}\). Literature on vascular access with ultrasound is contradictory about the best approach\(^{36,37,38,39}\), while available trials on peripheral blocks are mostly inconclusive\(^{40}\). In a direct comparison with 24 students on an ultrasound phantom, Meiser et al. found a significant difference in success and time with and without needle navigation, but not between in plane and out of plane insertion\(^{41}\). Another trial found needle guidance helpful for an out of plane approach by inexperienced sonographers but did not compare it directly to in plane\(^{42}\). Other authors found no superiority of a needle tracking system for in plane insertion in a blinded cross-over RCT on 26 volunteers\(^{43}\). It is indeed challenging but crucial, to visualize the needle tip in any approach\(^{44}\). Using an in plane approach, which is often presented as „best practice“\(^{34}\), the needle must be aligned perfectly parallel to the probe, but may in fact often be introduced slightly oblique. It is dangerous to misinterpret a part of the shaft for the needle tip, which is in fact some millimeters further, possibly causing damage. Furthermore, it is sometimes difficult to get the best picture of the needle and of the target structure at the same time, due to anisotropy of nerves. On the other hand, using an out of plane approach without being familiar with more complex techniques like the „walk down maneuver“ and identifying the more hyperechoic small double signal of the needle tip, the needle tip can very easily be pushed behind the scanning plane\(^7\). In practice, many people prefer an in plane approach in teaching, but we do not have any satisfactory evidence about the best introduction technique, neither in general, nor for each single block. Furthermore, there may be differences between single blocks and catheter insertion\(^{45}\). Needle recognition software (electronic beam steering) and technical solutions like „harmonic imaging“ (nonlinear propagation of the ultrasound waves through the tissue layers), “compound imaging” (multiple images of an object combined in one image) are available on most of the modern ultrasound machines, even if strong evidence of their efficacy is lacking. Furthermore, they show limitations in deep blocks. “Echogenic“ needles with polymeric coating may be helpful in both insertion techniques, when puncture angles become steeper than 30-45 degrees to the probe, but they are not ubiquitously available\(^{46}\). In obese patients, where the ultrasound beam is attenuated and problems with axial, lateral and temporal resolution and reverberation become more pertinent, „hydrolocation“ or „hydrodissection“ with minimal amounts of saline is useful to identify the needle tip and increase safety\(^{44,47,48}\) without deteriorating the quality of block\(^{49}\). Small amounts of fluid create a space to advance the needle further and serve as an acoustic window with dorsal enhancement. It is crucial not to have any air microbubbles in the syringe.

What are the evidence-based advantages of USGRA?

For more than 10 years there is an ongoing debate about the level of evidence on the advantages of ultrasound\(^{50}\). From the end of the 90s to the first decade of the 2000s, there have been multiple trials comparing USGRA and neurostimulation for different blocks. Major findings included\(^{25,51,52}\):

- Improved success of sensory blocks
- Decreased need for rescue analgesia
- Faster onset of the blocks / reduced time to achieve an effective block
- Speedier execution of the block
- Less procedural pain
- Less skin punctures
- Less vascular punctures
– Reduced amount and volume of local anesthetics needed
– Reduced incidence of Local Anesthetics Systemic toxicity (LAST)

The PERSEUS-RA guidelines by ESAIC emphasize the fact that there are only a few high-quality clinical trials and cohort studies and there is “remarkably little good evidence of this nature”\textsuperscript{25}. Hopkins questioned the need for such comparative trials in a remarkable editorial 15 years ago, citing several obvious benefits of USGRA\textsuperscript{53}. Considering the limitations of many trials, we decided to include the findings of previous systematic reviews. Liu et al. in an older systematic review, analyzing 14 RCTs and 2 case series with over 100 patients, reported a reduced number of attempts and shorter time to perform blocks with USGRA compared to neurostimulation. They reported improved block quality only in “some cases”. The efficacy of ultrasound guidance was high but not significantly better than with neurostimulation. In 2009, despite several small studies stating the opposite, the authors of this review concluded that ultrasound was not inferior but did not significantly improve the success of regional anesthesia. There wasn’t any data on nerve injuries, as no serious complications had been reported in the included studies\textsuperscript{54}. In contrast, another meta-analysis and systematic review of RCTs by Abrahams et al., also in 2009, found faster onset, higher success rate, longer duration and a relative risk reduction of 84\% for vascular punctures with USGRA compared to nerve stimulation, but data and sample size were not sufficient to show a reduction of nerve injuries and LAST\textsuperscript{55}. Munirama and McLeod, in a meta-analysis of over 2000 patients, found significantly less vascular punctures, reduced periprocedural pain and less need for analgesic rescue with a significantly improved block success rate (91.8 vs.82.8\%) when using ultrasound compared to nerve stimulation. In their review, combining ultrasound and neurostimulation did not show any further improvement\textsuperscript{56}. Schnabel et al. in a meta-analysis of perineural catheter placement with ultrasound vs. nerve stimulation found similar pain scores postoperatively, but reduced rates of accidental vascular puncture, which is relevant for patient safety to prevent LAST\textsuperscript{57}. More recently, Neal et al. investigated patient safety, i.e., local anesthetic systemic toxicity (LAST), nerve injury, and, in upper extremity blocks, pneumothorax and the incidence of hemidiaphragmatic paresis, focusing on data published since 2009 and on RCTs with more than 500 patients, Ultrasound reduced the incidence of LAST. Ultrasound reduced the incidence of pneumothorax in supraclavicular blocks. Hemidiaphragmatic paresis occurred more rarely but was still present. USGRA did not substantially reduce the incidence of regional anesthesia related nerve injury\textsuperscript{58,59}. Other trials confirmed the finding, that ultrasound guidance reduces the incidence of LAST by reducing (but not excluding) the probability of intravascular injection\textsuperscript{60}. Besides the reduced volume of local anesthetics needed, the most important safety improvement is the direct sight of LA distribution. If the spread is not detectable, the needle tip may be in a vessel. Injecting local anesthetics in small aliquots of 3 ml, and looking for correct distribution of the fluid around the target structure is the best possible prophylaxis against LAST and recommended in guidelines and textbooks\textsuperscript{5,61}. A study by Zhang et al. in 2019 found higher rates of LAST using ultrasound alone, compared to nerve stimulation. The authors suggested the combined use of ultrasound and nerve stimulation to lower the risk. This trial investigated only deep blocks (lumbar plexus block combined with posterior transgluteal sciatic nerve block), where it can be difficult to determine the spread of LA\textsuperscript{62}. Thus, even with ultrasound, written guidelines for the treatment of LAST must be available and every provider must know where the lipid solution is stored.

**What is the value of „dual guidance“?**

As discussed above, ultrasound is superior to locate nerves\textsuperscript{63,64}. In superficial, easy to visualize targets on the upper limb, using additional nerve stimulation (dual guidance), doesn’t improve success rates and may cause discomfort\textsuperscript{65,66}. This can be different in deeper blocks, where it is challenging to locate the nerve correctly and visibility is often bad due to the opposition between resolution and penetration depth (N. obturatorius, lumbar plexus block, transgluteal sciatic block)\textsuperscript{67}. Some authors suggest dual guidance as a safety tool for education and teaching, as most USGRA
beginners tend to advance the needle without correctly visualizing the tip$^{68}$. On the other hand, this is quite old data and sensible tissues like vessels or pleura can’t be detected by nerve stimulation. A recent review by Gadsden$^{69}$ summarizes the advantages of using nerve stimulation as a supplement to ultrasound. Gadsen, as well as Khurana et al. in an ASRA newsletter$^{70}$, argue that ultrasound and nerve stimulation are complementary to improve patient safety. “Protective nerve stimulation”$^{71}$ is an additional safety tool. Neurostimulation serves as a monitor against needle-nerve contact. A threshold as low as 0.2 mA accurately differentiates between extra- vs. intraneural needle tip position, but a current up to 0.5 mA could not rule out an intraneural needle placement$^{72,73}$. Protective nerve stimulation with 0.5 - 1.0 mA has been suggested to avoid nerves not reliably seen with ultrasound but anatomically in the path to the target$^{71,74}$. The ASRA advisory panel suggests a motor response < 0.5 mA should be interpreted as intraneural needle position$^{75}$. There are also some disadvantages of dual guidance. Analysis of retrospective data reports a higher incidence of multiple skin punctures but doesn’t provide data about an increased infection rate$^{76}$. Author authors found significantly prolonged procedure times$^{77,78}$. Furthermore, the safety of 0.5 mA to avoid nerve contact may be questioned, as there are older case reports and animal models with intraneural needle position and currents up to 1.7 mA, without any motor response$^{79,80}$. This could be especially pertinent in patients with underlying conditions like diabetes mellitus and at risk for nerve injuries. Furthermore, although studies showed faster learning curves for ultrasound than for nerve stimulation$^{64}$, some authors advocate for the role of dual guidance in the education of novices$^{69}$.

**What do we know about the incidence of nerve injuries and the role of ultrasound?**

In general, nerve injuries associated to regional anesthesia are a rare event, but data is very heterogeneous. In children with blocks performed under general anesthesia the risk of transient neurological deficits was 1.6- 3.6: 10000 and the risk of permanent neurological deficit from 0 - 0.4: 10000 with no difference between neuroaxial and peripheral blocks$^{81}$. In case series on persistent phrenic palsy after interscalene block, an incidence of 0.048% was reported$^{82}$, while a prospective observational study found an incidence of 1%$^{83}$. An Australian survey of more than 7000 blocks reported 0.4: 1000 block related nerve injuries with a 95% confidence interval ranging from 0.08 - 1.1:1000$^{84}$. The main problem of data on nerve injuries related to nerve blocks in general and to USGRA in particular is the fact that causality of regional anesthesia is often unclear as surgery, positioning, traction and tourniquet also cause peripheral nerve injury. Inflammation, vasoconstriction, hypothermia, electrolyte disorders, ischemia due to hypotension or pressure and preexisting conditions like Diabetes mellitus with neuropathy, alcohol or tobacco abuse, are common pathomechanisms. Patient, surgical and anesthetic factors contribute to nerve injuries, which are more common in upper than in lower limb blocks, while a higher incidence for proximal than for distal blocks is controversial and not supported by evidence. Nerve injuries related to peripheral nerve blocks are rarely permanent. The persistence of symptoms decreases from 3 to 6 months to one year$^{72,75}$. According to older retrospective data over a 10 year period, the incidence of neurological complications seems to be more dependent on the type of surgery and the patient’s condition than on nerve blocks$^{85}$. Nerve injuries are different from postoperative neurological symptoms (PONS), transient neurologic deficits lasting up to 2 weeks (mostly paresthesia), which can occur in 8%$^{86}$. There is no evidence that the use of ultrasound reduces the incidence of nerve injuries or PONS. Though the hypothesis of pressure induced nerve ischemia by high volumes of local anesthetic and thus a potential benefit of ultrasound thanks to reduced injection volume has been raised$^{87}$, there isn’t any confirming evidence. Needle-nerve contact with damage to the nerve vasculature and micro-hematoma, but especially injection of local anesthetics into fascicles leads to direct damage, ischemia and inflammation, depending on volume and concentration$^{88,89}$. Unfortunately, ultrasound is not accurate enough to differentiate reliably between intra- and extraneural needle position$^{90,91}$. No single nerve localization technique shows superiority in reducing the risk of nerve injury yet. Thanks to technical innovation, this may be subject to further investigation in the future$^{92,93}$. That’s why the use of nerve stimulation together with ultrasound as a safety feature...
has been advocated for, as discussed above. Nevertheless, we could not find any comparative studies to state an outcome difference in block related nerve injuries between USGRA alone and ultrasound with nerve stimulation.

**Can pressure control combined with ultrasound avoid nerve injuries?**

Monitoring further variables like pain during injection—though unreliable, as shown by old data—and injection pressure to avoid intraneural injection are recommendable. Injection pressure monitoring and limiting the injection pressure to < 15 psi can minimize the risk of nerve injury. High injection pressure is possibly a sign of intraneural injection and may lead to nerve damage. The subjective pressure evaluation (“syringe feel”) even of experienced anesthesiologists is unreliable and dependent on the needle type. An injection with compressing an air column over a fluid is the traditional technique to control injection pressure, but now commercial solutions are available. The ASRA practice advisory and the NYSORA group recommend a multi-modal technique to avoid potential nerve injuries, combining all 3 techniques of ultrasound, nerve stimulation and pressure monitoring altogether (“triple guidance, triple monitoring”). A pragmatical algorithm is available at. The current evidence suggest that all methods are complementary and a single best practice to avoid nerve injury can’t be recommended. A recent prospective observational investigating a multimodal approach is limited by the lack of randomization and blinding. Much of the evidence for risk factors of nerve injury comes from cadaver models, animal models and case reports and clinical relevance remains uncertain.

**Further ultrasound related approaches to avoid nerve injury**

Abouzied and Wilson question some of the ultrasound related established “best practices” with regard to patient safety. In fact, it has not been scientifically proved yet, that “circumferential” spread of local anesthetics around nerves is mandatory for a successful block. For some nerves like popliteal sciatic this may be advantageous according to a single center proof of concept trial on 64 adults. On the other hand, more needle manipulations near the nerve lead to more possible needle-nerve contacts and possible injury. Especially in a femoral nerve block or sciatic nerve block for postoperative analgesia combined with general anesthesia, a single local anesthetic depot lateral to the nerve is sufficient and may avoid trauma. Because of the previously explained difficulties to see the needle tip at any time, it seems reasonable to place the needle intentionally near, but not too close to the nerve, measuring opening pressure and looking at the local anesthetics spread, instead of aiming the needle directly at the nerve. In a cadaver model there was a statistically significant lower incidence of intraneural injections with a tangential approach compared to a direct approach to the nerve. Other authors suggest the use of ultrasound to stay farther away from the nervial borders altogether. We know that all local anesthetics can be neurotoxic to different degrees. As this is a dose dependent effect, reducing concentration and volume – a proved advantage of USGRA - may reduce the risk of nerve damage.

**Using ultrasound, is the awake, conscious patient still mandatory?**

Even with the use of ultrasound, current international guidelines recommend performing nerve blocks in an awake, conscious adult. Nevertheless, paresthesia or injection pain does not reliably indicate peripheral nerve damage, but reversely if a conscious patient complains about such symptoms, this must prompt cessation of injection and needle repositioning. However, in children or in patients at risk of movement during the procedure, performing the block under general anesthesia is not excluded or even recommended, if the benefit outweighs the risk. As shown in, it obviously does not provoke more permanent nerve injuries. To this date, the strongest argument to advocate for performing blocks in the conscious patient, is to minimize the risk for wrong-sided blocks (WSNB) as a part of the „stop before you
block” campaign. Furthermore, in conscious patients, neurological symptoms of LAST are easy to notice. Nevertheless, atypical presentations of LAST like cardiovascular symptoms without CNS symptoms or a delayed onset of symptoms after as long as 60 minutes are possible, as USGRA has reduced intravascular injections. Furthermore, in clinical practice, it seems clear that geriatric patients with dementia may benefit from an opioid sparing multimodal pain therapy concept including USGRA. Often, they do not fulfill the criteria of “consciousness” and tend to move a lot during the procedure.

**Are adjuvants necessary, useful and safe in USGRA?**

As many local anesthetics cause vasoconstriction to different degrees, the use of adrenaline can reinforce this effect and lead to ischemic nerve damage. Thus, at least according to animal studies, adrenaline as an adjuvant is not a good choice, especially around poorly vascularized nerves like the sciatic nerve or in patients with risk factors for neuropathy and microangiopathy like diabetes. Adrenaline increases the safe dose of local anesthetics with regard to LAST, but as discussed before, thanks to USGRA doses and volumes for most blocks have significantly decreased. Adrenaline as an adjuvant to local anesthetics can detect intravascular injection, but at least 15µg Adrenaline is necessary to detect a relevant increase in heart rate and blood pressure with limited reliability in pain, stress, with beta-blockage or in geriatric patients. So slow injection and meticulous observation of LA spread in real time ultrasound may be safer and more useful than adding adrenaline, without the risk of ischemia. Other common adjuvants are dexamethasone, clonidine and dexmedetomidine, opioids, ketamine and anti-inflammatory drugs (NSAID). The aim is to enhance efficacy of the block, prolong the clinical duration and reduce the dose of local anesthetics. Neither of them is per se neurotoxic but in vitro they showed different effects on the neurotoxicity of ropivacaine. The clinical significance of these findings remains unclear. All adjuvants have typical systemic side effects like hypotension and bradycardia and are off-label drugs for perineural use. Findings for clonidine are heterogenous while dexmedetomidine and dexamethasone prolong blocks significantly in clinical practice and dexmedetomidine didn’t show any neurotoxicity in animal models. Neither the action nor the side effects of adjuvants can be altered using ultrasound. Adjuvants and USGRA may be complementary in reducing the dose and thus potential neurotoxicity of local anesthetics.

**Are infections a problem specifically related to USGRA?**

Permanent nerve injury and loss of function may happen through infectious complications. There are many more case reports of disastrous complications like meningitis or abscesses in neuroaxial anesthesia than in US-guided peripheral nerve blocks. Data on ultrasound guided neuroaxial anesthesia is rather recent and no infectious complications related to the use of ultrasound have been reported. Most of the trials report lesser needle passes through the skin with ultrasound guidance. This could theoretically be an advantage. Nevertheless, the use of ultrasound equipment is a potential risk for infectious complications, so disinfection standards and barrier cautions are mandatory. In single shot peripheral nerve blockades, infectious complications are a very rare event. Catheter techniques have a higher incidence and demand a higher standard of hygienic barriers, but all this data is retrospective, mostly older and none of it directly related to the use of ultrasound. Most of the hygienic recommendations for USGRA are the same as for the insertion of central lines and the prevention of central line-associated bloodstream infections (CLABSI). The recommendations are conclusions by analogy from preventing bloodstream infections (BSI). Effectiveness of every single step is hard to assess, so a bundle approach is the method of choice. Bundles have provided evidence of infection prevention in different healthcare settings, so they should also be useful for USGRA. The German society of Anesthesiology and Intensive Care (DGAI) has published hygiene recommendations for regional anesthesia in 2006, updated in 2015 (“10 commandments”) and recently re-published in an educational...
Successful infection control is possible by following these recommendations. Some of these rules directly rely on the use of ultrasound. There is no data that using ultrasound per se leads to more infections. Nevertheless, to maintain an aseptic field for catheter techniques, it is essential to cover the probe and the whole cable with a long sterile sheath to avoid contamination of the puncture site or the needle. In single shot technique, a short cover of the probe or inserting the needle 2 cm away from the probe after correct skin disinfection is sufficient. There is no data comparing these two techniques, at least in teaching of novices we recommend using a short cover at any time. Sterile saline is the best choice to improve the contact to the skin and the image as needling through disinfectants is not advisable. Chlorhexidine with alcohol may be neurotoxic to an unknown extent. Needling through sterile gel may cause nerve inflammation, if gel is spread into the tissue. The results from different animal models are inconclusive. If gel is used, it should be single-use and sterile, as non-sterile, multiuse gel is a recently identified source of infections and outbreaks with opportunistic bacteria. After each patient, it is mandatory to clean and disinfect the ultrasound probe and the touch-screen/keyboard of the ultrasound machine with disinfecting substances authorized by the manufacturer. An Australian trial performed microbial tests for contamination of ultrasound equipment in the ICU and emergency departments, not directly related to regional anesthesia. They found a high rate of contamination and thus a possible risk of transmission of infectious diseases by ultrasound probes and machines, prompting national guidelines for reprocessing probes. Similar recommendations exist from the European Society of Radiology Ultrasound Working Group and the American College of Emergency Physicians.

**Is USGRA safe(r) in coagulation disorders?**

Hematoma is a long-known cause of nerve damage even in superficial peripheral blocks. Mandatory safety rules for known coagulation disorders or antithrombotic medication exist for many years, but the focus was on neuroaxial anesthesia and the rules for ultrasound guided peripheral nerve blocks and fascial blocks were only conclusions by analogy. Pharmacokinetics of antithrombotic drugs and case series of complications formed the base of recommendations. The incidence of neurological sequelae due to hematoma associated with neuraxial anesthesia varies from less than 1 in 150 000 for epidural anesthesia in labor and less than 1 in 220 000 for spinal anesthesia in obstetrics, to 1 in 3000 in elderly women undergoing orthopedic surgery. There are no trials yet directly comparing the incidence of epidural hematoma in neuroaxial anesthesia with or without ultrasound. Former meta-analyses on ultrasound guided epidurals found a lower incidence of traumatic punctures, skin punctures, needle redirections, postprocedural back pain, headache and failed blocks, as well as a higher first pass success rate, but didn’t report differences in the incidence of epidural hematoma. Even if real time imaging seems much safer than a “blind” puncture, the use of ultrasound does not exclude vascular punctures for sure and there is no data yet supporting the idea that the use of ultrasound can exclude the formation of hematoma after nerve blocks in patients with coagulation disorders. Thus, the very recent joint ESAIC/ESRA guideline is the best available approach to assess the bleeding risk, based on the pharmacological principle of half-lives of drugs, renal function, the question of a „traumatic puncture” and the very useful and pragmatical distinction in „superficial” (compressible) and „deep” blocks. It clearly states that ultrasound guidance does not modify the recommended time intervals in deep blocks or neuroaxial anesthesia. In superficial blocks these restrictions do not apply, no matter if USGRA, nerve stimulation or dual-guidance is used.

**Conclusion**

The introduction of ultrasound massively increased the interest in peripheral regional anesthesia. Several advantages of ultrasound are evidence based, but for patient safety, especially to prevent nerve injuries, ultrasound alone is not a “magic bullet” and a combination of techniques and safety measures is essential. Several questions remain open to investigation and the evidence is not very robust. New pathophysiological hypotheses on
nerve injury\textsuperscript{171} and the ongoing technical progress of ultrasound machines and needle guidance tools, as well as the unresolved question, how many and which of the different blocks are really useful in clinical practice, will demand further research.

**Contributors:** MHT contributed to conception, literature research and rating, writing and editing the final manuscript. NN raised valuable questions and contributed to writing and editing the final manuscript.

**Funding:** none

**Competing interests:** Financial: None. MHT is member of the scientific working groups „Regional Anesthesia“ and „Ultrasound“ of Deutsche Gesellschaft für Anästhesie und Intensivmedizin (DGAI), member of the European Society of Regional Anesthesia (ESRA), member of the Deutsche Gesellschaft für Ultraschallmedizin (DEGUM) and honorary member of the Serbian Association of Regional Anesthesia (SARA). NN is member of DEGUM and SARA.

**Patient consent for publication:** not required

**Data availability statement:** Data sharing not applicable as no data sets generated or analyzed for this review.

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