Complex Bone Augmentation and Implantation Procedures

In-Situ Liver Splitting for Oncological Liver Surgery: a German Innovation

Current Treatment Modalities for Trigeminal Neuralgia

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Managing Director

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Complex Bone Augmentation and Implantation Procedures
Background
An appropriate bony situation is essential for dental implant placement and bony support of soft tissues (pink esthetic). Loss of teeth often results in complex horizontal and vertical alveolar ridge defects. They demand advanced bone augmentation techniques for reconstruction.

Purpose
We present the different techniques and materials used in complex bone augmentation. Clinical cases show the application of the methods in the clinical setting.

Materials and Methods
We present current techniques and materials used in complex bone augmentations. Clinical cases show the application of the methods in the clinical setting. Applied techniques include: stabilized guided bone regeneration, autologous local block augmentation, modified techniques such as Gellrich shell technique, including piezosurgery, pelvic bone blocks, complex materials such as graft-derived bone blocks, and their unique handling problems.

Results
Successful basic principles are: reduction of cortical bone healing due to long remodeling time and possible late loss; extended application of materials with interconnecting porous system and particulate material resulting in fast healing analogous to cancellous bone; mechanical stabilization of the augmentation to allow bone healing in vertical defect situations.

Conclusions
Guided bone regeneration and autologous bone blocks with minimal cortical thickness and a high volume of particulate material are most favorable techniques.

Key words: dental implantology; bone augmentation; dental implants

I. BASICS
Bone Morphology
The two morphological forms of bone are cancellous and compact bone (36, 88) (see Fig. 1). Cancellous bone shows

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a trabecular structure with an internal lumen containing bone marrow that serves as a source for pluripotent stem cells and vessels during the healing process. Healing starts in a lamellar fashion from the bone marrow space. Cortical bone is a compact and stiffer structure with higher mechanical stability and limited internal remodeling capabilities. The internal structure of both bone tissues is lamellar as described above.

Histomorphology of bone distinguishes between lamellar bone of complex structure and plexiform bone (see Fig. 1) (36, 88). Plexiform bone does allow fast healing and growth but only simple structures of orthogonal primary osteon structure with a mechanical overall weakness of evolutionary relevance in large organisms. It is therefore often found in small mammals such as mice, rats, and some rabbits. Larger mammals including pigs, dogs, and humans have a complex lamellar bone structure. Ontogenesis of bone in humans starts with embryonal plexiform bone structures leading to the mature bone structure with secondary osteons (Haversian system).

The structure principle of compact bone consists of osteons with a central Haversian canal containing osteocytes and vessels, surrounded by mineralized matrix lamellae and interstitial lamellae (see Fig. 1) (88). Osteocytes are connected with each other via gap junctions through the Canaliculi ossei. Cancellous bone trabeculae are similar in structure.

Periosteum separates bone from surrounding connective tissue and consists of two layers: Stratum fibrosum (external) and Stratum osteogenicum (internal) containing nerves, vessels and also osteogenic progenitor cells allowing chemotactic migration during bone healing.

Fig. 1: Left: Bone morphology of compact and cancellous bone; right: Two-times sequence marking with tetracycline in the rabbit patellar groove model shows the lamellar bone healing.

The cover of dental implants is a challenging task. Although the number of implants is increasing, the demand for innovative solutions is also growing. Researchers are focusing on developing new materials and methods to improve implant integration and durability. The use of novel biomaterials and surface modifications is a promising approach to enhance implant osseointegration. Further advancements in surgical techniques and patients' oral health continue to play a critical role in the success of dental implants. The journal Dental Implantology aims to bridge the gap between clinical practice and scientific research, providing a platform for sharing knowledge and fostering collaborations among professionals in the field.
Bone tissue consists of cells and matrix (ossein). Ossein contains inorganic minerals, mostly hydroxyl apatite, and organic molecules mostly collagen type I, composed in a complex way to form a stable bone matrix structure (40, 104, 119, 136). The organic matrix also contains several other molecules with complex functions including proteoglycans such as aggrecan with its glycosaminoglycan arms and multiadhesive proteins, but also its hyaluronic acid cores or newly discovered fibrils and other structures under current research (39, 50, 96).

Bone Healing

Healing of augmented bone transplants and biomaterials at the interface site is analogous to defect fracture healing (2-4, 32, 35, 36, 47, 70, 71, 75, 93-95, 137): aseptic inflammation and chemotactic cell migration; loose preliminary tissue (soft callus); mineralized immature bone (hard callus); remodeling resulting in full functional bone (see Fig. 2) (105). This mode of healing concerns all free avascular transplants including guided bone regeneration (GBR) and block augmentations. Contact healing is therefore not an issue in all of these augmentations and would require both sides of the healing site to be vasculated vital bone tissue (see Fig. 2) (35, 88). The gap healing in bone augmentations includes lamellar healing at the interface site and the periostium with cell recruitment from blood, bone marrow and the periostium, depending on the type of defect (see Fig. 2) (2-4, 32, 35, 36, 47, 70, 71, 75, 93-95, 137).

Contact healing

- Havers channels jump the fracture gap
- CAVE: Remodelling is essential for full stability

Defect or gap healing

- A: Inflammation: A: hematoma / B: chemotaxis/migration / C: granulation
- B: Soft Callus
- C: Hard Callus
- D: Remodelling

Fig. 2: Synopsis of bone healing types; left: contact healing; right: gap and defect healing
on the local anatomy (see Fig. 3) (33-35, 79, 87).

This cell recruitment includes local osteoblast progenitors (human trabecular bone-derived cells - HTBs), and blood-derived CD-34-positive embryogenic progenitor cells (EPCs) (14, 74, 91, 111, 140). Differentiation of local adult stem cells is not well understood yet. However, the differentiation of EPC follows a stepwise change into an osteoblast while losing pluripotent capabilities from the EPC with high CD34-positive cells, followed by the stage of "circulating osteoblast lineage cell" towards the "blood mesenchymal precursor cell" (BMPC) directly differentiating into osteoblasts with continuously rising percentage of stromal cell-derived factor-1 (SDF-1) CXCR4 receptors (74). Vascular cells in newly formed bone tissue are also derived from EPCs (54, 60). Osteoclasts are part of the mononuclear phagocyte system and derived syncytia formations of these cell lineages (108).

Viscerocranial bone of the facial area is mesectodermal tissue derived from the branchial arch rather than mesenchymal tissue derived from other bones (22-24, 66). This issue should be considered.

Cell Induction in Bone Tissue: Osteoinduction and Neoangiogenesis

The time course of bone healing is influenced by several factors. This includes the stability and morphology of the transplant or mesh graft with biomaterial as well as biological factors. Those factors are osteoconductivity, osteoinductivity/vasoinductivity, and osteogenicity present in the bony implant bed and the graft or mesh.

Osteoconductivity concerns macro- and micromechanical, and morphological properties that promote a bone

with that in mind, we divide this section into different parts to explain the main stages of bone healing: subperiosteal healing (lamellar healing in the matrix) and contact healing at the interface. The implantation process includes the following stages: 3. Subperiosteal healing of an implant or transplant.

Fig. 3: Synopsis subperiosteal healing of an implant or transplant.
tissue-specific activity and differentiation including matrix-cell-interactions, but also pore size, surface properties, and interconnectivity of pores in biomaterials and bone grafts, but finally also external mechanical influences such as shock waves (13, 41, 52, 65, 90, 141).

Osteoinductivity is specific ligand-dependent cell activation by growth factors and other molecules leading to bone growth and differentiation. Growth factors are related to the TGF-β family, such as BMPs (bone morphogenic proteins) e.g. BMP-2 or BMP-7, or basic FGF and VEGF (2, 12, 55, 58, 59, 67, 126-129, 139). FGF and VEGF are also strong vasoinductive factors. There are several approaches to applying growth factors in clinics (11, 17, 45, 46, 68, 121, 122, 138). However, this application will most likely remain limited to specific clinical conditions for two main reasons. Firstly, tissue healing is limited by cell capabilities during the described phases of bone healing with cell recruitment, chemotaxis, differentiation, and specific tissue matrix production and cannot be accelerated beyond biological limits by external growth factors. Current experimental results do not respect these clinically relevant limits in vitro and in vivo (72, 105). Secondly, it is a fact that application of growth factors and their influence on adult and embryonic stem cells and differentiated tissues involves the risk of carcinogenic transformation (78, 85, 89, 92).

Osteogenic properties concern the continuity of living bone cells after transplantation. This is possible by using small bone pieces combined with fast revascularization (e.g. particulate bone augmentation), press-fit transplants in cancellous bone healing (clinically not relevant in oral & maxillofacial surgery), and microvascular transplants such as fibula or similar free flaps.

Signal transduction in bone cells includes general elements such as ras and MAP-kinases, but also Smad-dependent pathways and integrin-associated

- the osseous matrix used to facilitate
- the nanoparticle matrix used to release the growth factors
- the bone chips from the implant
- the bone mill for particularization of blocks

A: Bone chips from the implant
B: bone mill for particularization of blocks
C: bone scraper
D: commercial biomaterial (example: BioOss)

Asymmetric tissue or biomaterial activity and differentiation including matrix-cell-interactions, but also pore size, surface properties, and interconnectivity of pores in biomaterials and bone grafts, but finally also external mechanical influences such as shock waves (13, 41, 52, 65, 90, 141).

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signaling (29, 84, 109, 120). Smad-dependent signaling includes specific second messengers such as RunX2 and consists of a complex system of sub-elements depending on the associated ligand-system. BMPs activate Smad 1, 5 and 8 complex that binds Smad 4 and others as DNA-binding complex in osteoblasts (29, 84, 109). Integrins, on the other hand, represent an element of signal transduction activation by specific matrix binding (41, 65, 90).

II. BIOMATERIALS AND TRANSPLANTS

Bone Transplants and Alloplastic Biomaterials

We will not discuss the wide field of biomaterial products in-depth as already published elsewhere 28, 30, 106. Materials for bone augmentation are divided into alloplastic (artificial) biomaterials and transplants alongside with their natural xenogeneic, allogeneic, or autologous derivatives (16, 21, 37, 44, 48, 51, 64, 97, 101, 130, 131). Most common alloplastic materials are: β-tricalcium phosphate (97), bioactive glasses (101), and hydroxyl apatite (51). Bone material can be further characterized as: autologous (fresh or frozen), allogeneic (e.g. DBM “demineralized bone matrix”), and xenogeneic. Important material properties concerning bone healing are pore size and interconnectivity, resorbability without severe inflammation, and macrostability of particulate material (63). Some of these factors, such as pore size and surface properties, are evaluated scientifically, while other factors such as macrostability are mostly clinically based experiences (13, 141).

Materials can be further characterized by their potential to influence bone healing 3: osteoconductive (promotes bony ingrowth); osteoinductive (induces bone tissue generation by receptor-mediated cell activation); osteogenic (material contains living bone cells or bone cell precursors).

Most common particulate materials are bone chips: from the implant site, milled bone blocks, scraped bone chips, mesh grafts with alloplastic materials (see Fig. 4). Growth factors and tissue engineering

بعد المحددات الحيوية والعوامل الخارجية للأكثر
من النتائج التشريحيتية لا تحترم هذه
المحددات السريرية سواء في النسيج
الحي أو الزجاجي (2-50).

II. المواد الحيوية والعوامل
العظام العظمية والمواد الحيوية
البلاستيكية

لن تنافش الحقل الواسع للمشتقات
الحيوية بعقم تم نشرها في
مكان آخر (2006). 30. 31. 32. تقييم
المواد المستعملة لتجريب العظام إلي
صعيبة (نطيرة بلاستيكية
aluropenic bone chips حبة ثلاثية
الفاوسفات الكالسيوم
لاجع الحيوي (91) هيدروكسي
البيتهيد (51) والPROTOCAL
ECF.

وأخير:

علامات التبليغ في الخلايا العظمية
تتضمن انعصر عامة مثل:
كنينات MAP-kinases ras
وأيضا صادم متعدد على سبام
الاستردادات المتزامنة مع
 dumpster signaling (59) انترغرين
110. 110. 110. 110. 110. 110. 110.
وتتماشى انتشار المبتدأ

BMPs على

1 BMPs وتتالف من

نظام معقد يعتمد على

انعصر جزيئي متعدد على نظام مرتبط


are future options in compromised bone healing and complex reconstructive surgery (11, 12, 46, 53, 54, 66, 74, 112, 113, 124, 128, 129, 132-134). Problems of these techniques are costs and carcinogenic risks of growth factors (11, 12, 54, 74, 85, 89, 100, 132, 133). Dental implantology therefore offers limited indications for these options.

Donor Sites for Bone Transplants

Choosing the appropriate donor site for bone transplants is the second step after analysis of the defect and augmentation planning. Most common donor sites are (63):

- Mandible (chin, angle, linea obliqua, corpus mandibulae) (62)
- Maxillary (tuber, spina nasalis, crista zygomaticoalveolaris)
- Calvaria (tabula externa)
- Pelvic rim
- Tibia

Local donor sites are of special interest for applications in oral and maxillofacial surgery. Intraoral donor sites are shown to be less painful for patients (see Fig. 5) (76). Big defects require extraoral donor sites, mostly from the pelvic rim region. Quality and healing properties of various bone transplants concern their onto-

ان أهم الخصائص فيما يتعلق بالتنام العظم هو حجم الانتان الداخلي، فئوية الامتصاص بدون خمي شديد والاستقرار الكبير لمواد محدودة (13). يقين بعض هذه العوامل علميا مثل حجم وخصائص السطح، بينما العوامل الأخرى مثل الاستقرار الكبير يتعلق بالدرجة الأولى على قواعد وخبرات سريرية (141, 13).

يمكن ان تمتاز المواد أيضا حسب قدرتها الكامنة على التأثير على النمو العظمي (3) الناقلية العظمية (تسمى بالنمو العظمي osteoconductive) أو النسج العظمي (osteinductive) وتتضمن توليد النسيج العظمي بتفعيل الخلايا بواسطة المستقبلات، مواد الطعام (3) تحتوي على خلايا عظمية حية أو طلاع الخلايا العظمية) وأغلب المواد الخاصة الشائعة هي رقائق عظمية من مواد مماثلة للبلاستيك (شكل 4).

**Dental Implantology**

Fig. 6: Osteotomy techniques
A: Situation before osteotomy after previous augmentation and resorption of the bone block after 2 years
B: Situation after osteotomy
C: osteotomy gap after the simultaneous implantation (Nobel Biocare Replace-base)
D: crestal view after implantation;
E: Result after osteotomy and implantation

الشكل 6: تقنيات قطع العظم
A: الحالة قبل قطع العظم بعد تكييف سابق وارتفاع العظم لكتلة عظمية بعد سنتين
B: الحالة بعد قطع العظم
C: الفجوة الناجمة عن قطع العظم بعد الزرع بنفس الوقت
D: منظر العرق بعد الزرع
E: النتائج بعد قطع العظم والزرع

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Fig. 7: Bonesplit
A: simultaneous splitting and implantation
B: result after bonesplit and implantation (Zimmer Dental Implants)
Fig. 8: Stable GBR technique with titanium mesh

A: adjusting to the vertical defect (Tiolox Mesh), fixation and augmentation (Bio-Oss)
B: vertical defect initial
C: after surgery
D: result after 4 months
E: implantation after mesh removal (Straumann)
Bone augmentations in dental implantology can be classified according to various definitions (80). We suggest the following systematic order for complex bone augmentations:

- **Osteotomy techniques:**
  - distraction osteogenesis,
  - sandwich techniques, bone split
  - particulate techniques: stiff guided bone regeneration (GBR)
  - block techniques: blocks and lamellae

**Osteotomy Techniques**

The main advantage of all osteotomy techniques is the preservation of the crestal soft tissue, especially the attached gingiva and in some cases even the papillae. All osteotomy techniques involve the risk of fractures in the treated area.

Pelvic rim

- harvesting bone from the pelvic rim is the method of choice for most indications requiring large amounts of autologous bone since it involves limited risks and allows good access (61, 81, 99). There is an anterior and posterior approach (38, 61, 81). It has been discussed that the less common posterior approach may offer more bone and less morbidity (1, 61, 81). Complications of this donor site are pain, bleeding, nerve lesions (N. cutaneus femoris lateralis), and fractures of the pelvic bone (61).

**III. COMPLEX BONE AUGMENTATIONS – GENERAL TECHNIQUES**

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Mandibular

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pelvic rim

- harvesting bone from the pelvic rim is the method of choice for most indications requiring large amounts of autologous bone since it involves limited risks and allows good access (61, 81, 99). There is an anterior and a posterior approach (38, 61, 81). It has been discussed that the less common posterior approach may offer more bone and less morbidity (1, 61, 81). Complications of this donor site are pain, bleeding, nerve lesions (N. cutaneus femoris lateralis), and fractures of the pelvic bone (61).

**III. COMPLEX BONE AUGMENTATIONS – GENERAL TECHNIQUES**

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Distraction osteogenesis is an interesting technique in dysgnathic and craniomaxillofacial surgery (114). Several approaches in dental implantology have been published (9, 125). The main problems limiting wide applications are two facts:

1.) If there is enough bone for a distractor, it is also enough for a dental implant.

2.) The distraction device leads to additional costs. However, there are some indications for alveolar alignment. But these cases can mostly also be solved by a sandwich technique with lower costs and without the discomfort of the distraction process.

Sandwich techniques are analogous to distraction.

A gap is created by placing the fragment in the final position and fixed with either osteosynthesis material or the implant itself, instead of callus distraction from a small gap (102, 103) (see Fig. 6). Costs and morbidity are limited compared to distraction.

Bone split is a horizontal osteotomy technique mentioned here for completeness of the methods. A narrow alveolar ridge can be widened and simultaneous implantation is possible (see Fig. 7). The technique is especially interest-
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Fig. 11: Bony healing after 4 to 6 months; A: GBR techniques achieve a complete healing as well as lamellar block technique; B: Classic block does not achieve a complete bone remodeling in time, but interface is usually not close to the implant axis; C: cylinder transplant with smooth interface unfavorably close to the implant axis; far right side: clinical example cylinder transplant with loss after 10 months.

Techniques separating the particulate material from the surrounding soft tissue (19, 25, 26). The membrane has three functions: stabilization of the material, barrier towards the surrounding soft tissue, limitation of resorption (19). Most common membrane materials are xenogeneic collagen (49, 142).

Applying this technique to complex vertical defects requires a stable membrane, usually made of titanium or metal-en-
forced alloplastic membranes (e.g., PTFE). The membrane becomes adapted to the dedicated planned augmentation area and is filled with particulate augmentation material (see Fig. 8) (18). The application of the described stiff and non-resorbable membranes requires a removal procedure usually combined with the insertion of the dental implants.

Practical problems of titanium membranes include fibrous ingrowth through the wide holes, especially in situations with less autologous bone, and the risk of exposure of the membrane through the gingiva. Using a collagen membrane additionally limits both risks. Removable prosthetics should avoid pressure in the augmentation area. Metal-enforced alloplastic membranes are occlusive and can also lead to exposure of the membrane due to blood supply problems. Avoiding perioistal cuts and crestal approaches is one option to limit risks.

All cases require an appropriate safety distance from surrounding teeth and the associated infection risks from the periodontium. GBR technique can be combined with other techniques such as block augmentations. The main problem of particulate techniques is the

in these cases can be solved with a GBR technique with lower costs and without additional surgery (Fig. 12). An advantage of this procedure is the ability to reduce bone resorption. In situations with less autologous bone, the risk of membrane exposure through the gingiva is minimized. Using a collagen membrane can further reduce these risks. Removable prosthetics should avoid pressure in the augmentation area. Metal-enforced alloplastic membranes are occlusive and can also lead to exposure of the membrane due to blood supply problems. Avoiding perioistal cuts and crestal approaches is one option to limit risks.

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Fig. 13: Fixed prosthetics immediately after implantation with tilted implants ("All-on-4"; "Malo technique")
A: planning with Nobel Clinician
B: result after surgery
C: immediate prosthetics in situ

Block Techniques

Classic block augmentation uses an autologous transplant block fixed with either an osteosynthesis screw or the dental implant itself.

Block material can be:
1. Local bone transplants from the facial bone,
2. Distant donor regions (calvaria, pelvic rim, tibia),
3. Commercial materials such as allogeneic or xenogeneic bone material.

The concept allows three applications of the block: modified shell technology with thin bone block and combined particulate material, classic hand-formed blocks, and cylinder transplants.

Modified shell technique (lamellar block) applies a thin cortical bone transplant (e.g. from the crista zygomatico alveolaris) being filled with particulate material analogous to GBR techniques (see Fig. 9 and 10) (42).

Classic block technique applies an appropriate block being adjusted to the local situation fixed with osteosynthesis screws or the implant itself. Edges are smoothed and particulate material is applied at the rims (64).

Using cylinder blocks is a less common technique mostly involving autologous cortical transplants (31). Further observation of these cases revealed negative results. The main problems from our point of view are: interface at the peristodontium and the correlation to the alveolar bone. Reliability of the interface is assessed by the quality of the callus formation and the incorporation of the cylinder block into the bone.

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The time-intensive and technical approach, and implant design are also important issues in block augmentation but not the focus of this review.

We give an overview of the block techniques and our recommendations compared to Gellrich-shell technique (lamellar block) and classic bone block and do not recommend cylinder transplants (see Fig. 11). We have limited data concerning resorbable cylinders with trabecular structure.

Crestal material rings around a dental implant are a modification of the cylinder techniques (43). The ring can consist of autologous bone or a biomaterial. This option may be more promising, since healing times are less important due to the one-step approach concept. The time-intensive and technically challenging surgery must be weighed against the other, simpler block techniques.

Collagen membranes can be applied in all block techniques to separate the soft tissue and allow neo-periosteum formation. We recommend the Gellrich-shell-technique and the classic bone block. Soft tissue management, surgical approach, and implant design are also important issues in block augmentation but not the focus of this review.

IV. COMPLEX BONE AUGMENTATIONS – APPLICATIONS

The Bony Defect after Tooth Loss in Dental Implantology

Bony defects are a common indication for preimplantological surgery (21, 37, 64, 130). Tooth loss leads to bone resorption in the jaws (20, 21, 37, 69, 130, 135). The degree of resorption, bone quality, and patient-specific factors demand specific bone augmentation techniques and bone graft donor sites. Classification of Cavood and Howell as well as imaging of patient-specific defects is the diagnostic basis for implant and augmentation planning in the indication groups (20, 21). Complex bone defect situations can be classified in indication groups:

- The bony defect is not surrounded by soft tissue (e.g., vestibular wound, etc.).
- The bony defect is surrounded by soft tissue and is covered by a mucosa flap.
- The bony defect is recorded by X-ray imaging in coronal view.
- The bony defect is not recorded by X-ray imaging in coronal view.

The application of augmentation bone grafts and various bone substitute materials in dental implantology is well described. Also autologous bone or a biomaterial is possible in augmentation of bone defects (43). The ring can consist of autologous bone or a biomaterial formed from the residual bone (42). The ring is alternatively possible a biological bone substitute.

Conclusion

Augmentation bone grafts and bone substitute materials in dental implantology are well described. Also autologous bone or a biomaterial is possible in augmentation of bone defects (43). The ring can consist of autologous bone or a biomaterial formed from the residual bone (42). The ring is alternatively possible a biological bone substitute.

References

The primary issue in edentulous jaws is the concept of removable versus fixed prosthetics. The bone resorption of the jaws leads to a prognathous mandible and loss of transversal bone width in the maxilla additional to the local bone resorption according to the classification of Cawood and Howell (21). These factors lead to a possible demand for bone augmentations. Rare cases with a wide alveolar ridge and solitary jaw base disparity are indications for a LeFort I osteotomy. This is usually combined with block augmentations from the pelvic rim. But most edentulous cases are indications for classic pelvic bone blocks in combination with large sinus floor elevations in the maxilla (see Fig. 12). A 3D backward planning is recommendable, since prosthetic and surgical planning is difficult to align without. Augmentation in the mandible is usually only necessary in the areas distal from the mental nerve, as described later.

Alternatives to bone augmentation are concepts using tilted implants to achieve a wide polygon for the fixed prosthetics with usually four or six implants, thereby avoiding contact to the maxillary sinus and the inferior alveolar nerve (see Fig. 13) (5, 73). Our results correspond to the published data and showed successful outcomes.

Front Teeth Area

The loss of front teeth, especially in the maxilla, leads to fast vertical and horizontal bone resorption (27, 123). This process begins with the thin anterior wall, which is often already lost or compromised at the time of tooth loss due to

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- Front teeth area
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Front Teeth Area

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periodontitis or trauma. Vertical bone resorption follows over time. Physiological differences in the time course of bone resorption include gender, ethnicity, and metabolic disorders. Socket preservation concepts involving biomaterial implantation as well as soft tissue transplants and flaps are applied to address this issue (57). Outcomes are not convincing in general, which leads to the need for bone augmentations in most cases (27, 123). These augmentations are usually done with classic bone blocks or shell block technique, as described above. Membrane techniques and sandwich osteotomy are also possible with indications in cases of limited vertical bone loss (membrane techniques) and wide alveolar ridges (sandwich technique). A planned immediate implantation is an alternative (see Fig. 14). Anatomically adapted implants can support this technique (see Fig. 15). Combination with immediate prosthetics is possible (82, 83). Other studies with negative results used other implant designs and must be critically considered (6-8).

Sinus Floor Elevation

The maxillary upper molar region shows specific bone resorption dynamics after tooth loss without periodontitis-associated vertical bone loss. Bone resorption takes place as a widening of the maxillary sinus with a vertical bone loss from this area without change of the alveolar crest. The correct bone augmentation in these cases is therefore an elevation of the sinus floor (107). There are two techniques. The first one involves a direct sinus floor elevation with a window approach.

Fig. 16: Block augmentation in the upper molar region combined with sinus floor elevation
A: block harvesting from the linea obliqua
B: Fixation with osteosynthesis screws
C: sinus floor elevation, smoothening of edges and particulate augmentation (BioOss)
D: result after surgery
E: result after 4 months
F: Implantation in the augmented area and additional immediate implantation after extraction of tooth 12 (Dentsply Implants OsseoSpeed)

Ruff Cauda obliterata
• Tegument the assever sins in the upper molar region
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Cawood and Howell (21)

Dental Implantology
infections or trauma can lead to Periodontitis, other severe infections in the Maxilla. Alveolar Ridge Augmentation

Implant bed according to Summers (116, 117). The second technique for sinus lift procedures is the indirect bone healing (115). Techniques involve classic block, lamellar block, or GBR techniques with autologous, allogeneic, or xenogeneic materials (see Fig. 16). Vertical osteotomy techniques are of limited value. However, the bone split is a classic technique in horizontal bone defects in the maxilla. Short implants can be an alternative (98).

Alveolar Ridge Augmentation in the Mandible

Lateral vertical bone loss is a common problem in the mandible. The most common and simple procedure is an interforaminal approach for removable prosthetics to avoid the absolute vertical bone defects in the maxilla. These defects require a vertical alveolar rim reconstruction in addition to sinus floor elevation. Prosthetic analysis should ensure correct planning of these augmentations. Techniques involve classic block, lamellar block, and GBR techniques with autologous, allogeneic, or xenogeneic materials (see Fig. 16). Vertical osteotomy techniques are of limited value. However, the bone split is a classic technique in horizontal bone defects in the maxilla. Short implants can be an alternative (98).

from the anterior maxillary wall as described by Boyne and Tatum (15, 118). This approach can involve a bony window swinging inside the sinus while the membrane is preserved and detached from the basal bone (62). A modification of this approach is an osteoplastic window by removing the facial bone completely for the preparation of the sinus membrane (10). A biomaterial membrane can be used to cover possible defects in the sinus membrane (10). The created space can be filled with ceramics, bone, or a mesh graft. Some authors showed that augmentation is not necessary, but one must consider the effect of a biomaterial filling for potentially faster bone healing (115). The second technique for sinus lift procedures is the indirect elevation of the membrane with osteotomes through the drilled crestal cavity of the implant bed according to Summers (116, 117).

Alveolar Ridge Augmentation in the Maxilla

Periodontitis, other severe infections or trauma can lead to

ملفـ 17: زيادة العظم باستعمال الكتل في منطقة الرضح السفلي (Zimmer Dental Puros)

- A اطباق مواد الكتل

- B التثبيت، تلصيف الحواف، زيادة العظم باستعمال الجرينات (BioOss) بفضل BioGide

- C النتائج بعد 4 أشهر (Zimmer Dental) 

D و E الزرع

منطقة الرضح السفلي

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Alveolar Ridge Augmentation in the Maxilla

Periodontitis, other severe infections or trauma can lead to


Difficult augmentations. Bone augmentations in the lower molar region are often required if fixed prosthetics are planned. This area involves the inferior alveolar nerve and is therefore challenging. The alveolar rim is often thin and requires horizontal augmentations as well.

Appropriate techniques in cases without vertical loss involve small particular augmentations without membrane, GBR techniques, or tunnel technique approaches.

Bone augmentations with block material of any kind, stiff membrane GBR, or osteotomy techniques can be applied in cases with vertical bone loss (see Fig. 17). Short implants are also an option, as mentioned above.

Suspension and horizontal interforaminal bone augmentation in the lower tooth-bearing area is an option, as mentioned above. Short implants are also an option, as men- 

See Fig. 17). Short implants in cases with vertical bone loss techniques can be applied in membrane GBR, or osteotomy block material of any kind, stiff bone augmentations with techniques, or tunnel technique approaches.

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In-Situ Liver Splitting for Oncological Liver Surgery: a German Innovation

Keywords: liver resection, two-stage hepatectomy, postoperative liver failure

To avoid postoperative small-for-size syndrome or liver failure after right trisectionectomy for a malignant lesion, a sufficient liver remnant, in terms of volume and function, should be ensured upon the time of surgery (1). Portal vein embolisation (PVE) of the right portal branch to induce hypertrophy of the left liver followed by right trisectionectomy a few weeks later has been successfully applied for the treatment of hilar cholangiocarcinoma (CCA) (2,3). Following the same concept, PVE or portal vein ligation (PVL) of the right branch with wedge resection of all left-sided tumours followed by right trisectionectomy in the second stage has been applied to increase the resectability of bilobar colorectal liver metastases (CRLM) (4-6). Beside PVE is not always technically feasible due to tumour extension, two drawbacks of this strategy have been noted:

1) patients with locally advanced inoperable disease, which could only be discovered intraoperatively, might undergo unnecessary PVE because the decision is made according to the preoperative image (5) and 2) patients might experience disease progression during the waiting time until sufficient hypertrophy of segments 2 and 3, possibly caused by the methodology itself (7).

To induce rapid hepatic hypertrophy with intraoperative ad-hoc decision-making, a novel concept has been recently developed in several German centres to overcome the abovementioned drawbacks of conventional PVE/PVL (8).

This procedure was designated ALPPS (Associating Liver Partition and Portal vein Ligation for Staged hepatectomy) (9). The principle of the new strategy is deportalisation of liver segments 4 to 8 by combining PVL of the right portal branch with parenchyma transection along the falciform ligament as done in situ liver splitting for a left lateral graft. This method led to a 74% increase in the volume of the remnant liver in a mean of 9 days with a 100% tumour resection rate (8).

حقن تنازير الكبد صغير الحجم ما بعد الجراحة أو صور الكبد بعد الاستئصال المقاطع الثلاث للكبد الأيمن لمعالجة الأذى الحادة.

1. يتجنب التأكد على بقاء بقايا كبدية كافية من حيث الحجم والوظيفة عند وقت الجراحة (1).
2. يمنع تحويل التصفيق الوريد البابي لفروع وريد الباب الأيمن من أجل تحريض ضخامة الكبد الأيسر. يتبع ذلك قطع الفصول الوريدية والتي بعد عدة أسابيع

وذلك لمعالجة كاريومو الأقنية الصفراوية السريعة (CCA) (2). وبإتباع نفس المبدأ، فإن تصنيم PVL وربط الباب اليميني بربط الباب اليساري للفروع الوريدية التي مع القطع الأسفلية لجميع أورام الكبد السريرية مtrinsic

بقطع الفصول البدنية الثلاث في المرحلة الثانية. تم تطبيقها وذلك لزيادة إمكانية استئصال الانفقات الكبدية لسرطان الكولون والمستقيم (CRLM) (6). بالإضافة إلى ذلك تصنيم وريد البدن ليست ممكنة دائما بسبب امتداد الورم، فإن عاملين محظوين لهذه الاستراتيجية وهما:

1. المرضى الذين لديهم داء موضعي متقدم غير قابل للجراحة

Innovation

In-Situ Liver Splitting for Oncological Liver Surgery: a German Innovation

Keywords: liver resection, two-stage hepatectomy, postoperative liver failure

To avoid postoperative small-for-size syndrome or liver failure after right trisectionectomy for a malignant lesion, a sufficient liver remnant, in terms of volume and function, should be ensured upon the time of surgery (1). Portal vein embolisation (PVE) of the right portal branch to induce hypertrophy of the left liver followed by right trisectionectomy a few weeks later has been successfully applied for the treatment of hilar cholangiocarcinoma (CCA) (2,3). Following the same concept, PVE or portal vein ligation (PVL) of the right branch with wedge resection of all left-sided tumours followed by right trisectionectomy in the second stage has been applied to increase the resectability of bilobar colorectal liver metastases (CRLM) (4-6). Beside PVE is not always technically feasible due to tumour extension, two drawbacks of this strategy have been noted:

1) patients with locally advanced inoperable disease, which could only be discovered intraoperatively, might undergo unnecessary PVE because the decision is made according to the preoperative image (5) and 2) patients might experience disease progression during the waiting time until sufficient hypertrophy of segments 2 and 3, possibly caused by the methodology itself (7).

To induce rapid hepatic hypertrophy with intraoperative ad-hoc decision-making, a novel concept has been recently developed in several German centres to overcome the abovementioned drawbacks of conventional PVE/PVL (8).

This procedure was designated ALPPS (Associating Liver Partition and Portal vein Ligation for Staged hepatectomy) (9). The principle of the new strategy is deportalisation of liver segments 4 to 8 by combining PVL of the right portal branch with parenchyma transection along the falciform ligament as done in situ liver splitting for a left lateral graft. This method led to a 74% increase in the volume of the remnant liver in a mean of 9 days with a 100% tumour resection rate (8).

حقن تنازير الكبد صغير الحجم ما بعد الجراحة أو صور الكبد بعد الاستئصال المقاطع الثلاث للكبد الأيمن لمعالجة الأذى الحادة.

1. يتجنب التأكد على بقاء بقايا كبدية كافية من حيث الحجم والوظيفة عند وقت الجراحة (1).
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1. المرضى الذين لديهم داء موضعي متقدم غير قابل للجراحة
Indications
The potential candidates of ALPPS are patients who require a right trisectionectomy due to bilateral liver metastasis, intrahepatic cholangiocarcinoma and hepatocellular carcinoma with local invasion around the portal bifurcation (8, 10).

The type of major hepatectomy is determined according to the preoperative abdominal imaging and tumour staging including CT or MRI. Mainly is the right trisectionectomy, with or without wedge resection at the left lateral liver lobe.

Evaluation of the future remnant liver, namely, future remnant liver volume to total liver volume ratio (FLV/TLV) and future remnant liver volume to body weight ratio (FLV/BW), by a radiologist together with a liver surgeon should be carried out first. When an insufficient future liver remnant after one-staged surgery was expected (FLV/TLV< 25%, or FLV/BW< 0.5% in patients with a normal liver or < 30% and 0.8%, respectively, in patients with cholestasis or post-chemotherapy), an ALPPS procedure could be considered.

In patients with insufficient volume increase after PVE, ALPPS could still be an option to increase the future remnant liver volume (12).

Fig. 1: The right portal vein and main portal vein are exposed by lifting the common bile duct and right hepatic artery using a lid retractor. The arteries are slung with the red rubber bands.
Surgical Procedure
The first operation (right portal vein transection and in situ liver splitting)

During the first operation, an exploration is carried out to exclude extrahepatic tumours. Resectability is determined when the remnant segments 2 and 3 have adequate inflow as well as outflow. Tumour invasion of segments 2 and 3 alone is not a contraindication when it could be safely resected without tumour residual.

The next step is the dissection of the hepatoduodenal ligament. A cholecystectomy is optional. In patients without tumor infiltration of the gall bladder, a cholecystectomy is usually carried out. After lifting the common bile duct and right hepatic artery by a lid retractor, the right portal vein and main portal vein is exposed (Fig. 1). At this stage, the main right portal vein branch could be transected after suture ligation at the distal end and continuous suture with 5/0 Prolene at the proximal end. In patients with trifurcation of the portal vein with separate entry of the right anterior and posterior sectional branches, the anterior and posterior portal veins should be divided separately.

The umbilical portion of the left portal vein is exposed by dissecting the umbilical fissure. The portal branches of segment 2 are ligated. At this stage, a decision is made whether to split the left lateral lobe. The falciform ligament is kept in the future remnant side for fixation of the left lateral lobe at the diaphragmatic dome.

The second operation (bile duct resection and cholecystectomy)

The bile duct is resected using the CUSA along the falciform ligament (Fig. 2). The common bile duct and right hepatic duct are dissected and identified with rubber bands. The falciform ligament was kept in the future remnant side for fixation of the left lateral lobe at the diaphragmatic dome.

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When there is no isolated lesion in the left liver, the resection is made along the falciform ligament. The right hepatic artery, the main bile duct and the right hepatic vein are dissected and identified with rubber bands. The falciform ligament was kept in the future remnant side for re-fixation of the left lateral lobe at the diaphragmatic dome.

Fig. 2: Liver parenchyma transection using CUSA along the falciform ligament is performed along the falciform ligament. The right hepatic artery, the main bile duct and the right hepatic vein are dissected and identified with rubber bands. The falciform ligament was kept in the future remnant side for re-fixation of the left lateral lobe at the diaphragmatic dome.
Liver Surgery

Liver Surgery

The patient is usually transferred to the intermediate care unit and then discharged to the normal ward according to the postoperative course. Prophylactic antibiotics are given as single shot intraoperatively. If any bacteria are isolated from the intraoperative swab, the antibiotics should be given till the second operation. In patients with stented bile duct, antibiotics and antimycotics are given during the whole postoperative phase.

One week after the operation, depending on the logistics, an abdominal CT scan (native phase) is performed for re-evaluation of the liver volume (11). When the FLV/TLV is more than 30%, the second operation, namely, right trisectionectomy with or without bile duct resection, could be carried out on the next available operative day. If the FLV/TLV is less than 30%, repeat CT scan would be carried out in an interval of seven days, with the second operation being postponed accordingly.

The second operation (definitive right trisectionectomy)

After relaparotomy, the silicone sheeting or plastic bag is removed. An intraabdominal swab is taken for microbiological analysis for orientated antibiotic therapy if indicated. The hilar structures are easily identified by the rubber bands.

One may expect a period of healing before the patient can be discharged to the normal ward. Prophylactic antibiotics are given as single shot intraoperatively. If any bacteria are isolated from the intraoperative swab, the antibiotics should be given till the second operation. In patients with stented bile duct, antibiotics and antimycotics are given during the whole postoperative phase.

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The second operation (definitive right trisectionectomy)

After relaparotomy, the silicone sheeting or plastic bag is removed. An intraabdominal swab is taken for microbiological analysis for orientated antibiotic therapy if indicated. The hilar structures are easily identified by the rubber bands.
The right hepatic artery, the right hepatic ducts (or the left hepatic duct when extrahepatic bile duct should be resected), the right and middle hepatic veins are transected. Liver segment 1 could be preserved in patients with non-hilar CCA when there was no tumour involvement.

After removal the transected liver, a lymphadenectomy could be performed at this stage. Biliodigestive anastomosis is followed when resection of the extrahepatic bile duct is indicated in patients with intrahepatic CCA and hilar CCA.

The postoperative treatment after the second operation is same as for the patients undergoing routine major hepatectomy.

Perspective

A rapid hypertrophy of the left lateral liver lobe within one week is constantly reproducible by different liver centers worldwide (8-12). In some cases, the sufficient remnant liver could even be achieved 3 days after ALPPS (12). The procedure has been found efficient. First, the dearterIALIZED but arterialized right hemiliver, left in place, acts as an auxiliary liver to assist the future liver remnant for the first and critical week after resection (10).

Posthepatectomy liver failure could be thus avoided, even in patients having extensive exposure to chemotherapy with associated liver damage. Second, the rapid hypertrophy of the liver remnant within two to three weeks avoids tumor progression to an inoperable status, which could be found in conventional two-staged hepatectomy without ALPPS (4,5). No other techniques could achieve such a rapid hypertrophy within 2 weeks. No tumor progression has been found during this short period. This strategy may also allow a faster recovery for the patient, with the possibility of restoring chemotherapy earlier.

Recently, the authors extended the original ALPPS as left lateral splitting (liver splitting is carried out along the right side of the falciorm ligament in) to a full left-full right splitting (liver splitting was carried out along the Cantile line) (Fig. 3) to remove bilobar CRLM in a single hospital stay. This procedure provides a new strategy for treatment of bilobar colorectal liver metastasis. Using this one of the most promising advances in oncological liver surgery, we can provide many patients, who are with might otherwise be judged unresectable disease, with new chance by increase the resectability.

When there is an absence of more than FLV/TLV 30% it is an indication for the second operation. The second operation is performed in patients who have no or minimal hepatocellular damage, and who are in a good general condition. The second operation can be performed under local anesthesia, and the patient can be discharged on the day of the operation. Postoperatively, the patient is kept in the hospital for 3 days and then discharged.

The postoperative treatment after the second operation is the same as for the patients undergoing routine major hepatectomy.

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Liver Surgery
Along with the high efficiency on induction of hypertrophy of remnant liver, the ALPPS procedure showed significant postoperative morbidity (68%) and mortality (12%) in unselected patients (8). The authors have found that the patients with preoperative biliary strictures receiving biliary drainage carry a higher risk compared to other patients, as infection and bile leak are two main complications after ALPPS (11).

A dilated intrahepatic bile duct, bacterial contamination due to preoperative stenting and difficult hilar dissection at the second step can limit applying this strategy in patients with hilar CCA. As recommended by international expertise, this complex procedure must be undertaken exclusively by experienced HPB surgeons in a high-volume center, and by means of a multidisciplinary team effort, such as optimal management of anesthesiology recovery, hemodynamic development, antibiotics, early enteral/parenteral nutrition, and other issues to achieve the best results (11).

The CT scan at 7 days after full left-full right splitting liver splitting was carried out along the Cantile line, identified by the intrahepatic clips) to remove bilobar CRLM which involved all 8 liver segments. The CRLM at the segment 2 to 4 has been removed at the first operation as well as the segment 1.

The combination of the Cantile technique in the liver's left side, with the use of clips inside the liver, can identify the line for liver splitting. This technique involves the use of clips that are placed inside the liver, and then removed to create a split in the liver. This technique is particularly useful for removing tumors that are located in the left and right lobes of the liver.

The authors have found that patients with preoperative biliary strictures receiving biliary drainage carry a higher risk compared to other patients, as infection and bile leak are two main complications after ALPPS (11). The ALPPS procedure involves the removal of the left and right lobes of the liver, and the use of clips to create a split in the liver.

The ALPPS procedure is a complex procedure that must be undertaken exclusively by experienced HPB surgeons in a high-volume center, and by means of a multidisciplinary team effort, such as optimal management of anesthesiology recovery, hemodynamic development, antibiotics, early enteral/parenteral nutrition, and other issues to achieve the best results (11).
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Liver Surgery

The Journal of Medicine for the Worldwide Med Community

Literature


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Department of Hepatobiliary Surgery and Visceral Transplantation University Medical Center Hamburg-Eppendorf Hamburg

In addition to the functional data, in treatment of patients with primary sclerosing cholangitis and liver cirrhosis, ALPPS showed a significantly higher mortality rate compared to patients with other causes of liver failure. The ALPPS technique has been considered as an excellent method for achieving liver transplantation in cases of liver failure. Patients undergoing ALPPS showed a significant improvement in liver function and survival compared to the control group (12).
Silicone Implants for Breast Augmentation – a Review

Breasts are an important part of female identity. They are considered to be the symbol of femininity and fertility. Their size and shape vary greatly from person to person. Hypomastia, asymmetry, anomalies or the loss of the breast as a result of a mammary carcinoma can impair the self-esteem of women. Breast surgeries have been playing a leading role in the statistics of aesthetic interventions for years.

The following review is aimed to provide information about the possibility of breast augmentation using silicone implants, its history as well as the risks and complications associated with silicone implants.

History of Breast Augmentation with Silicone Implants

Breast implants were first mentioned in literature in 1895. The Austrian-German physician Vincenz Czerny removed a lipoma from a patient’s back and used its adipose tissue for breast augmentation (1). Cronin and Gerow were the first to describe and introduce breast implants made from silicone in 1963 (2). After this, the structure of silicone implants continuously changed. Today, we can look back on a total of four implant generations.

Between 1963 and 1988, nearly 1 million women underwent a breast augmentation with silicone gel implants in the USA alone (3). To this day, breast augmentation with silicone implants (both using silicone gel and saline solution) has been considered one of the most frequently performed interventions in plastic surgery, so far in an estimated 10 – 12 million women worldwide (4).

However, silicone implants, especially those filled with silicone gel, used to be highly disputed because evident studies investigating their safeness and health consequences were missing. The regulation and approval of such procedures in the USA is incumbent upon the Food and Drug Administration (FDA). This agency was given the authority over silicone implants in 1976 by virtue of the Medical Devices Amendment to the Food, Drug, and Cosmetic Act. Initially, in January 1963 (2), and in December 1976, the FDA approved the use of silicone gel implants (both using silicone gel and saline solution) for breast augmentation with silicone (1).

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ary 1992, the FDA recommended not to use such implants, predominantly because it was not possible to exclude the supposed correlation with the development of basic systemic diseases such as collagenosis (3). This was followed by a ban on implants filled with silicone gel on 16 April 1992, since many manufacturers had not followed the advice to avoid using silicone, and the safety of its use had not been proved. From that point in time, the use of implants was reserved for certain patients and breast reconstruction (5). Consequently, the number of augmentations with silicone gel implants in the USA dropped while implants filled with saline solution were increasingly gaining significance in clinical routine.

In 1995, the American College of Rheumatology confirmed that there was no correlation between the use of silicone gel implants and the development of collagenosis and rheumatoid diseases (6). This was followed by a statement of the American Academy of Neurology in 1997, postulating the safeness of implants in connection with neurological diseases (7).

In September 2005, after reviewing all studies and consulting with implant manufacturers, the FDA officially re-introduced silicone gel implants to the American market subject to certain restrictions (3). Although the official permission to use silicone implants was given, they remained disputed throughout the world. The complications have still not been completely clarified. During the last few years, large-scale retrospective studies were conducted to prove their application safety (8-15).

However, it still remains to be seen what complications, especially long-term consequences, are attributable to the use of implants.

Breast Augmentation is Indicated for a Great Number of Diagnoses

- Hypomastia
- Asymmetry / Anisomastia
- Anomalies and reconstructions following amputations

Table 1

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FDA in the beginning of 1993 authorized to use implants and disclosed a notification that some implants, produced by a number of manufacturers, had not been approved and that long-term complications could not be ruled out. This was followed by a ban on implants filled with silicone gel on 16 April 1992, since many manufacturers had not followed the advice to avoid using silicone, and the safety of its use had not been proved. From that point in time, the use of implants was reserved for certain patients and breast reconstruction (5). Consequently, the number of augmentations with silicone gel implants in the USA dropped while implants filled with saline solution were increasingly gaining significance in clinical routine.

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In September 2005, after reviewing all studies and consulting with implant manufacturers, the FDA officially re-introduced silicone gel implants to the American market subject to certain restrictions (3). Although the official permission to use silicone implants was given, they remained disputed throughout the world. The complications have still not been completely clarified. During the last few years, large-scale retrospective studies were conducted to prove their application safety (8-15).

However, it still remains to be seen what complications, especially long-term consequences, are attributable to the use of implants.
Hypomastia can either be congenital or occur in the form of involutional atrophy, frequently after pregnancy. Restoration of symmetry is indicated at a weight difference of approx. 200 g. In this case, either unilateral augmentation or reduction mammoplasty of the contralateral side can be performed (often separately). Breast augmentation can also be indicated for anomalies such as amazon syndrome (mammary gland development disorder) or Poland’s syndrome (development disorder of the upper extremity including mammary hypoplasia).

Preoperative Measures Prior to Breast Augmentation

Preoperative diagnostics should involve examinations of asymmetry and skin elasticity. Space-occupying masses are to be excluded through palpation. The axillary lymph node status is also to be clarified in the course of this examination. Mammography is additionally recommended over the age of 30. Furthermore, preoperative measures include photographic documentation and the marking of the planned incisions including orientation lines (e.g. median line).

Extensive preoperative consultation serves not only to inform the patient about the specific complications, but also to exclude special contraindications:

- If the family history reveals predisposition to breast cancer, it must be considered that implants complicate imaging diagnostics (particularly when the implant is positioned under the glands). An increased risk of breast cancer occurrence in implant wearers has not been verified in studies conducted so far.
- Already diagnosed breast cancer: This also constitutes a relative contraindication. If radiotherapy is envisaged, the increased rate of complications should be pointed out. Augmentation should be generally advised against, also because it may make it more difficult to identify local recurrences.
- Unrealistic expectations: The postoperative result may be expected to be different from the actual result.

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unsatisfactory, especially in the case of involutional atrophy following pregnancy (referred to as snoopy breast, involving lowering of the gland and the soft tissue envelope)

• Previous autoimmune diseases (cf. systemic complications!)
• Previous infections (mastitis)

Selecting the Implant
At present, silicone implants in Germany may be implanted in accordance with the “Essential Requirements of the European Directives” and must have a CE marking.

Implants differ regarding their shell, filling substance and shape.

The shell, which is still made of silicone, can either be smooth or textured (Fig. 1). Silicone implants Vulcanised with polyurethane are also available. A new approach is constituted by silicone shells coated with biocompatible materials (see below).

Besides saline solution, cohesive silicone gel is available as filling material.

Approaches
There are four possible approaches for breast augmentation: inframammary, periareolar (Fig. 2), axillary and transareolar. Each variant involves both advantages and disadvantages and should be selected according to the anatomical conditions and the patient’s expectations, besides the preference of the surgeon.

The inframammary approach is popular with many surgeons, in particular due to its good visibility during the surgery – and also during later interventions in case complications occur. This method involves an incision of approx. four cm in length made two fingers caudal Regarding the shape of the implants, a distinction is made between round-high, round-low and anatomical profiles.

Anatomically shaped implants have the typical drop shape. It should be considered that the shape of the augmented breast substantially depends on gravity and the pressure in the soft tissue, which are both subject to dynamic change.

طريقة تكبير الثدي
هناك أربع طرق ممكنة لتلك كبيرة:
الثدي: تحت الثدي (شكل الثدي، ما حول الثدي، شكل الوعاء (شكل الثدي، ما حول الثدي، شكل الوعاء، عبر الوعاء، عبر الوعاء، عبر الوعاء، عبر الوعاء. كل طريقة تمثل فوائد وأضرار و يجب اختيارها حسب الظروف التشخيصية وطلب المريض، بالإضافة إلى رغبة الجراح.

ان طريقة الزرع تحت الثدي هي شائعة لكثير من الجراحين، وخاصة بسبب البداية الجيدة خلال الجراحة، وأيضا خلال التدخلات اللاحقة. يتم في هذه الطريقة إجراء جرح بطول 4 سم فوق الثدي تحت الثدي (Fig. 3: Intraoperative specimen of a severe capsular fibrosis)

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Implant Positioning and Surgery Technique

The implant site can be either subglandular or submuscular. In addition to better soft tissue coverage of the implant, submuscular positioning involves lower risk of capsular fibrosis development. Mammograms can also be better assessed when positioning the implant this way (16). Submuscular positioning involves exposure of the caudal edge of the pectoral muscle and its manual preparation. The cranial mobilisation is continued up to the third rib. Lateral detachment is performed up to the front or median axial line, depending on the implant size. The bottom edge of the pectoral muscle is medially detached from the sternum. During preparation, it should be taken into account that complete muscle coverage usually results in the implant being positioned too high. After inserting trial implants and checking the symmetry, the implant size is determined and the implant is inserted after being rinsed with saline solution, as far as possible, without touching the previously disinfected wound edges. The wound is subsequently closed layer by layer; Redon drainages may be applied where necessary.

Postoperative Measures

During the postoperative phase, excessive physical strain such as housework, sports and also physically demanding occupational activities should be avoided. Full, unrestricted physical strain should not take place until four months after surgery. A special bra exerting caudal pressure to avoid cranialisation of the implant should be worn for six months. Depending on the implants selected, the patient should do massage exercises directly after surgery. In contrast to coated implants, which should not be moved excessively, early massage is advantageous with smooth implants to avoid capsular fibrosis. The implants should be pushed in a medially directed manner. During the postoperative phase, excessive physical strain such as housework, sports and also physically demanding occupational activities should be avoided. Full, unrestricted physical strain should not take place until four months after surgery. A special bra exerting caudal pressure to avoid cranialisation of the implant should be worn for six months. Depending on the implants selected, the patient should do massage exercises directly after surgery. In contrast to coated implants, which should not be moved excessively, early massage is advantageous with smooth implants to avoid capsular fibrosis. The implants should be pushed in a medially directed manner.

The preparation of an adequate implant site is considerably more difficult with the periareolar and axillary approaches. Moreover, the incision through the gland may lead to cicatisation and the possible destruction of the lacteal ducts. The axillary approach involves the risk of implant lateralisation.

Surgery Technique

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to the existing inframammary fold, so that the resulting scar is located in the later mammary fold and is not visible in upright position.

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Possible Complications of Silicone Implants

The use of silicone implants may involve systemic and local complications. This list is intended as an overview only. The information in the literature relating to the incidence of complications varies considerably and is largely dependent on the surgeon’s experience.

Systemic Complications

The occurrence of systemic complications in connection with silicone implants gave rise to controversy. Especially the connection between the development of collagenoses, such as systemic lupus erythematosus, scleroderma, Sjögren’s syndrome or rheumatoid arthritis and the use of silicone implants are subject to debates (17, 18).

This supposed correlation also led to silicone gel implants being banned by the FDA (see above). However, large-scale studies were unable to establish a connection between the use of silicone implants (both filled with silicone gel and those filled with saline solution) and the development of diseases that belong to the group of collagenoses, autoimmune diseases and rheumatoid arthritis (3, 17, 19-21).

The influence of silicone implants on the development of cancer has been discussed for years. The main focus of attention in this context is breast cancer; however, further malign anomalies such as sarcomas, haematopoietic malign diseases as well as cervical, vulvar, lung and cerebral tumours are also suspected of being caused by silicone implants. Several epidemiological studies demonstrated no influence of silicone implants on the incidence of tumour-associated diseases (17, 22, 23).

Although small-scale case studies demonstrating a correlation between the use of silicone implants and rare types of cancer are available, this correlation, if true, would contradict the results of large-scale studies demonstrating no connection between the use of silicone implants and the occurrence of systemic complications such as sarcomas, haematopoietic malign diseases as well as cervical, vulvar, lung and cerebral tumours. However, further research is needed to clarify this issue.

The use of silicone implants may also involve local complications such as infection, implant rupture, migration, calcification and disintegration. If the slightest suspicion of an implant rupture arises, sonography and, if necessary, also MRI should be conducted.

During the initial phase after surgery, checkups should take place at close intervals, which should be followed by checkups after 3, 6 and 12 months and subsequently once a year. During these checkups, changes in the implant position should be monitored by means of photographic documentation. If the slightest suspicion of an implant rupture arises, sonography and, if necessary, also MRI should be conducted.

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has so far not yet been verified in large-scale studies (3).

Local Complications
Alongside local infections, particularly postoperative haematomas and seromas are counted among local complications. Another problem is posed by the sensation of local tenderness on pressure and pain (17). Wound infections occur in less than 5% of all patients (3, 24). In some cases, the implant needs to be removed again and can only be reinserted after the infection has subsided to ensure complete healing (3). In this case, the procedure is determined on the basis of the results and the surgeon’s experience. Wound infections after implantation occur twice as often as following reconstructive surgery than after implant change or a simple breast augmentation (25).

Further complications include the development of haematomas. Their incidence is stated to be 5% on average (3, 24) and seems to be not dependent on the type, filling material, surface texture and position of the implant. It is reported that the occurrence of haematomas involves a twofold higher risk of capsular fibrosis (25).

Implant ruptures involve silicone migration into the surrounding tissue and the risk of capsular fibrosis. The risk of implant rupture increases along with the period of implantation, the risk being highest 11-26 years following the implantation (26). The symptoms of implant rupture can vary greatly. In some cases, it manifests itself through nodulation, lowering of the breast, asymmetry as well as pain or a feeling of tension. The migration of silicone gel (gel bleeding) into the surrounding tissue is not always necessarily the consequence of an implant rupture. Silicone gel may also leak out of the implant shell without it showing any signs of a rupture. In addition to the above-described process, silicone particles of the implant shell may also decompose. The silicone fragments induce an inflammatory foreign-body reaction in the tissue (17). Furthermore, it is described that

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Fig. 4: Series of pictures of a patient status post bilateral mammary carcinoma, bilateral reconstruction using autografts and silicone implants, now high-grade (Baker III) capsular fibrosis of the left breast.

a and b: preoperative images, c: Intraoperative image showing the implant, d: postoperative result, patient fully recovered.
silicone fragments may also form so-called silicone granulomas and pseudotumours, which deposit in both the local lymph nodes and the surrounding tissue (17, 27).

The most frequently discussed local complication that may occur after the implantation of silicone implants is the fibrotic enclosure of the tissue, the consequence being capsular fibrosis.

The physiological reaction of the body to a foreign particle that is too large for phagocytosis involves the formation of a capsule of connective tissue. This capsule completely encloses the foreign particle, for example silicone implants, and holds it in place. In some cases, however, this capsule changes, it hardens and contracts (Fig. 3). The result is referred to as capsular fibrosis or capsular contraction (28, 29) (Fig. 4a-d).

The incidence of capsular fibrosis is greatly divergent in the current literature; it varies between 4 and 74% (24, 30-32).

In spite of substantial efforts to reduce the incidence of capsular fibrosis, a second, under certain circumstances even a third, surgery is required in 5-10% of the cases involving either capsulotomy or implant removal/change.

The causation of capsular fibrosis is still unknown and disputed; however, various influence factors are known and have been described:

1) Various Filling Materials
Both implants filled with saline solution and those filled with silicone gel are reported to have certain advantages (3, 25, 31, 33). In clinical practice, the filling material used usually depends on the surgeon’s preference.

2) Position of the Implant (Submuscular Versus Subglandular)
The position of the implant and the consequences for the development of capsular fibrosis are also subject to heated debates in the literature (34). For example, Vazquez et al. report an incidence of capsular fibrosis of 58% in the submuscular position.

In the subglandular position, however, this incidence decreases to 34%.

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The most frequently discussed local complication that may occur after the implantation of silicone implants is the fibrotic enclosure of the tissue, the consequence being capsular fibrosis. Fig. 4b: Preoperative image

 debido a la reducción de la cantidad de grasa en los tejidos alojados en los parches de grasa. El resultado es una mejoría en la adherencia de los implantes al organismo, lo que permite una mayor estabilidad y un mejor resultado estético.

En conclusión, la cirugía de implantes de silicona puede ser un procedimiento seguro y efectivo, siempre y cuando se realice de manera adecuada y se cumplan los protocolos de seguridad establecidos. Es importante que los pacientes sean evaluados por un especialista antes de someterse a la cirugía y que se realicen controles periódicos para supervisar el resultado final. De esta manera, se puede garantizar un resultado satisfactorio y seguro para el paciente.
lar contraction of 9.4% with submuscular implantation and 58% with sub glandular implantation (16).

These insights are contradicted by latest studies conducted with substantially larger cohorts. Handel et al., for example, see no connection between the implant’s position and the development of capsular fibrosis (25).

(3) Bacterial Population
The bacterial population of implants seems to constitute one of the main risk factors. The main focus of attention in this context is Staphylococcus epidermidis. Naturally occurring in the skin flora, this germ is increasingly found in the duct system of the female breast and can be isolated in the secretion of the glands surrounding the mamilla and the breast parenchyma (34). Staphylococcus epidermidis is capable of forming a biofilm, thus attaching to exogenous materials. This biofilm appears to be the starting point for irritations and the main stimulus for the fibrotic enclo-

sure of the capsular tissue (35). This biofilm is far more common in patients with capsular fibrosis of the implants. In addition to the presence of coagulase-negative staphylococci (Staph. epidermidis), an increasing occurrence of propiobacteria and corynebacteria is observed with manifest capsular fibrosis (36).

(4) Surface Texture of the Implant
During the last few years, the surface texture of silicone implants and its influence on complications have increasingly become the focus of attention. Silicone implants were coated with polyurethane as early as the end of 1960. The main advantage expected was the reduction of incidence of capsular fibrosis. This surface vapour deposition was very controversial because there were concerns over possible toxic effects of polyurethane. In their retrospective study, Handel et al. (31) investigated the complications and advantages of these implants and ascertained a dramatic reduction in the incidence of mucor granulopathy Slurpinell ulceration and wound healing defects, propiobacteria and corynebacteria and ascertained a significant reduction of incidence of complications and adverse effects. Handel et al. (31) investigated the complications and advantages of these implants and ascertained a significant reduction of incidence of mucor granulopathy Slurpinel.

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Fig. 4c: Intraoperative image showing the implant.
capsular fibrosis. Vazquez et al. made similar observations; they found a capsular fibrosis incidence of less than 1% in retrospective (37). Toxic complications were not verified, however, carcinogenic factors were suspected. This type of implant had been implanted in about 110,000 women in the USA until it was removed from the market in 1991 due to the suspected carcinogenic factors. Today, implants coated with polyurethane are frequently used in Brazil (37, 38).

During the last few years, smooth and textured implants were repeatedly compared in the literature regarding their complication rates. The introduction of textured implants was expected to improve biocompatibility and reduce the complication rate compared to conventional smooth implants.

The rough surface was supposed to promote the formation of collagen networks, which were expected to stabilize the implant and protect it against shear forces (39). Furthermore, a lower incidence of capsular fibrosis was expected. The improvement of biocompatibility through the textured silicone surface has already been described in previous studies; latest studies confirm this finding (30).

Wong et al. (30) reported in 2005 that the use of textured silicone implants can reduce the incidence of capsular fibrosis in the early postoperative phase. The positive effect of the rough surface on the development of capsular fibrosis has, however, not been confirmed in long-term studies (28). Hence, the actual advantage is still questionable. Vapour deposition or coating of the silicone surface with various materials and substances constitute a new approach. The primary goal is to find substances that are capable of both reducing infections and improving the biocompatibility of silicone.

A study presented in 2010 compared the biocompatibility of silicone implants vapour-deposited with halofuginone (32). Wong et al. (30) reported in 2005 that the use of textured silicone implants can reduce the incidence of capsular fibrosis in the early postoperative phase. The positive effect of the rough surface on the development of capsular fibrosis has, however, not been confirmed in long-term studies (28). Hence, the actual advantage is still questionable. Vapour deposition or coating of the silicone surface with various materials and substances constitute a new approach. The primary goal is to find substances that are capable of both reducing infections and improving the biocompatibility of silicone.

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lactate with that of conventional silicone implants. Animal experiments revealed indications of improved biocompatibility and a reduction of incidence of capsular fibrosis (40). The same study group was also able to ascertain that the coating of implants with phosphorylcholine has the same positive effect, alongside its additional anti-inflammatory effect (41).

Another study conducted in 2010 used silicone coated with copper and was able to verify reduced bacterial population of the surface compared to conventional silicone (42). An influence on the formation of the capsule was not found.

Prospects
The coating of the silicon shell with biocompatible materials is an interesting new approach. In this respect, coating the implant shell with titanium is a particularly promising method (43, 44). In their animal experimental studies, Bergmann et al. were the first to ascertain an advantage of the titanium coating of silicone shells: Both reduced inflammatory foreign-body reaction and a changed capsular architecture was demonstrated. The capsule was considerably less sensitive to irritation (43). Of course, this animal experimental approach needs to be verified in large-scale clinical studies.

Summary
Breast augmentation using silicone implants still constitutes a possible way of breast reconstruction. It is the method of choice especially aesthetic surgery patient. The continuous further development of implants and surgery techniques has made it possible to reduce the number of complications on a global scale. The type of breast augmentation and particularly the type of material and surgical method are still substantially dependent upon the respective surgeon’s experience and assessment.
Plastic Surgery
THE JOURNAL OF MEDICINE FOR THE WORLDWIDE MED COMMUNITY

Literature


3. Gamper T, Juhlin L, Conroy W, Morgan RF. Silicone gel implants in breast augmentation and reconstruc-


7. Ferguson JH. Silicone breast implants and neurologic disorders. Report of the Practice Committee of the


9. Strock LL. Two Stage Expander Implant Reconstruction: Recent Experience Breast Reconstruction Supple-

10. Heden P, Bronz G, Elberg JJ, Derae-


5;28(2):75-9.


23. Zeisler H, Laera-Avelaneda A, Schmidt K. Surface modification of silicone breast implants by bonding the antifouling coating heparin to polyurethane foam to prevent capsular fibrosis. Plastic and reconstruc-
tive surgery. [Comparative Study Research Support, Non-U.S. Gov’t]. 2010 Jul;126(1):266-74.

24. Gouas M, Prando L, Feldman M, Kottak A, Hnaberg S, Burgers R. The effects of copper additives on the quantity and cell viability of adher-


Summary
Classical trigeminal neuralgia is caused by vascular compression of the trigeminal nerve. Pain control can often be achieved by antiepileptic medication. Interventional procedures should be considered in case of insufficient effect or intolerable side effects. The actual review summarizes the current treatment guidelines and the results of the different modalities. The positive long-term experience after vascular decompression confirmed the causal concept of vascular compression. Idiopathic trigeminal neuralgia has become curable, in principle, by the microvascular decompression according to Jannetta. Radiosurgery by means of Gamma Knife has achieved an accepted place in the treatment of those patients who are no candidates for surgery because of their general health or age. Percutaneous thermocoagulation and glycerol infiltration are also proven methods for these patients. Radiosurgery and percutaneous procedures share the disadvantage of sensory loss and a 50% recurrence rate within 5 years. The choice of an intervention adapted to the individual patient is possible today. Disadvantages of the minimal invasive procedures are sensory deficits and high recurrence rates.

Key words: Trigeminal neuralgia, microvascular decompression, stereotactic radiosurgery, thermocoagulation, glycerol infiltration

Introduction
Trigeminal neuralgia is a lightning, extremely intense, electrifying and stabbing pain in the distribution of one or more trigeminal branches defined (4). The attacks typically hold in seconds and occur both spontaneously and triggered by stimuli such as touch in the face, chewing, talking, swallowing or brushing teeth. The pain is disabling and agonizing. Eating often becomes impossible. Therefore, trigeminal neuralgia must be treated with medication immediately. Multiple attacks can occur daily initially for episodes of weeks to months and then disappear again for weeks to months. Usually, the course is progres-

الأنظمة العلاجية الحالية لألم العصب مثل التوائم

الخلاصة
إن ألم العصب مثل التوائم التقليدي يحدث بسبب الانضغاط الوعائي على العصب مثل التوائم. ويمكن الحصول على تسنين الألم باستخدام أدوية مضادة الصرع. ويمكن الأخذ بعين الاعتبار لاستخدام التداخلات في حال عدم وجود تأثير علاجي أو وجود تأثيرات جانبية لادورية تقوم بالمراجعة الحقيقية بتصنيف التوجيهات العلاجية الحالية. تنتهي الأنظمة المختلفة وإن الخبرات طويلة الأمد الإيجابية بعد إزالة الانضغاط بالوعية قد أثبت المسبب بالانضغاط الوعائي للعصب مثل التوائم فلقد أصبح الألم عصب مثل التوائم البديني قابل للعلاج وكبداأ بانعمل المشرف غاما (الجراحة العصبية) قد حصلت على مكان مقبول في معالجة مؤل للمريض والذين لا يمكن أجراء الجراحة لهم بسبب حالاتهم الصحية العامة أو تقدم العمر.

ولقد تم اكتساب فائدة استعمال التنظير الحاري أو التصميم بالغليسروا للآفات المرضية. وتتشاكل المعالجة بالجراحة...
sive, although a few patients have only one episode in their lifetime.

The so-called idiopathic or classic trigeminal neuralgia is due to a vascular compression of the trigeminal nerve at its origin from the brain stem (1). The conflicting artery, most often the superior cerebellar artery can often be identified using advanced MRI diagnosis (6).

Significant developments have taken place regarding treatment in recent years. On the one hand, the positive long-term experience with microvascular decompression of the nerve (Jannetta's procedure) confirmed the concept of vascular compression as the cause of classical trigeminal neuralgia convincingly (1). Thus, trigeminal neuralgia became a curable disease. On the other hand, radiosurgery using Gamma Knife has gained a firm place in the treatment of patients who cannot have surgery because of the general condition or age. The aim of this review is to draw a current balance on the results of the various methods of intervention and to discuss the specific indications. Recommendations for drug therapy are oriented according to the guidelines of the German Society of Neurology.

Drug Therapy
Also in 2012, the initial treatment approach should be conservative. Basically, a surgical procedure should be considered when a drug maintenance therapy leads to significant side effects or if it results in inadequate controls neuralgia. The side effects of all medications that are effective for trigeminal neuralgia, consist of dizziness, drowsiness, cognitive impairment through to MRI visible cerebral and cerebellar atrophy. For the non-drug treatments such as psychotherapy, acupuncture and dental care.

In the field of medical journals, the treatment of patients with trigeminal neuralgia has undergone significant progress in recent years. On the other hand, the positive long-term experience with microvascular decompression of the nerve (Jannetta's procedure) has been convincingly (1). Thus, trigeminal neuralgia became a curable disease.

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In the treatment of trigeminal neuralgia, appropriate pharmacotherapy is still rather empirical than evidence based. Treatment with carbamazepine is known worldwide despite a plethora of available newer antiepileptic drugs. 90% of patients respond well to initial treatment with carbamazepine. Target dosage is 600-1200mg per day. Plasma levels should be monitored at higher dosages. Target levels are 4-12 mg/l. Besides fatigue, ataxia and occasional cognitive impairment, skin rash, thrombocytopenia, leucopenia, hepatic dysfunction and cardiac arrhythmia rarely occur as side effects.

Oxcarbazepine, a prodrug of carbamazepine acts like carbamazepine in trigeminal neuralgia. It is rapidly absorbed with a maximum serum concentration after one hour. Required dosage is 900 to 1800 mg/d. Fewer cognitive side-effects and the lack of autoinduction are considered advantageous in comparison with carbamazepine. On the other hand, the incidence of hyponatraemia is higher with oxcarbazepine, about 23% (16). Regular lab checks are therefore necessary and attention should be paid to clinical symptoms of hyponatraemia such as dizziness, headache, fatigue or nausea.

By contrast, surgical intervention is decreasing. Given the small therapeutic effect, however, (10). With time, this initial good effect often responds well to treatment, especially in early disease.

Classical trigeminal neuralgia is inadequately controlled by pain medication or if the side effects of drug therapy produce a substantial limitation in quality of life.

Because of the very short duration of attacks, beginning medication after onset of the attack comes too late. Therefore, it must be the aim of preventing the occurrence of painful attacks by an appropriate prophylaxis.

The medication dosage must be individualized according to the effects and side effects. Starting with a low dosage, medication is increased until satisfying pain control is achieved or intolerable side effects occur. When the effect wears, dose modifications are required. Conversely, when no pain occurs at a given dosage for more than 1-2 months, gradual dose reduction should be considered.

Classical trigeminal neuralgia, especially in early disease, often responds well to treatment with anti-epileptic agents (10). With time, this initial good therapeutic effect, however, is decreasing. Given the small number of randomized controlled trials, the selection of appropriate pharmacotherapy is still rather empirical than evidence based. Treatment with carbamazepine is known worldwide despite a plethora of available newer antiepileptic drugs. 90% of patients respond well to initial treatment with carbamazepine. Target dosage is 600-1200mg per day. Plasma levels should be monitored at higher dosages. Target levels are 4-12 mg/l. Besides fatigue, ataxia and occasional cognitive impairment, skin rash, thrombocytopenia, leucopenia, hepatic dysfunction and cardiac arrhythmia rarely occur as side effects.

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A number of other substances have been proposed for trigeminal neuralgia. These include baclofen, lamotrigine, gabapentin, pregabalin, valproic acid, and tricyclic antidepressants. It is important to note, however, that currently only the substances carbamazepine, gabapentin and pregabalin are licensed for the indication “trigeminal neuralgia” or “neuropathic pain”.

Sometimes exacerbation of attacks asks for acute pharmacological intervention. This can be achieved by slow intravenous administration of 250 mg of phenytoin. The rate of administration should not exceed 1 mg/kg/min due to cardiodepressant action. The subsequent dosing is prescribed as 3mg/kg body weight i.v. or p.o., t.i.d.

The evidence for anti-epileptic drugs for trigeminal neuralgia appears sufficiently established. In contrast, typical pain medications such as non-steroidal anti-inflammatory drugs and opioids are little effective.

**Microvascular Decompression**

Following the guidelines of the German Association of Neurology, surgical treatment in classical trigeminal neuralgia is indicated when either drug therapy is unsuccessful or if the side effects affect quality of life significantly.

The microvascular decompression after Jannetta is now accepted as a curative treatment (1). This is an intervention in the posterior cranial fossa through a small suboccipital incision.
Microvascular decompression may lead to a sensory deficit in the face, but, as expected, less frequently than the destructive methods, such as radiosurgery and percutaneous thermocoagulation, etc.

Radiosurgery Treatment (Gamma Knife)
During the last decade, Gamma Knife radiosurgery has gained a certain place in the treatment of trigeminal neuralgia (7). The method is less invasive than microvascular decompression and can be accomplished under local anesthesia. Here, the trigeminal nerve is irradiated with a single dose of 80-90 Gy close to its exit from the brainstem (Fig. 3). Radiosurgery is an ablative method that leads to partial damage of the nerve. Therefore, 10 - 30% of patients get a significant sensory deficit. Neuralgia is initially relieved in 70-90%, with the relapse rate of 15% of the patients. Rarely, the Teflon cushion may become displaced. If there is a relapse after microvascular decompression, the primary response should be to reestablish drug therapy. In case of inadequate pain control or substantial side effects we recommend a surgical revision, or other interventional procedures.

Although microvascular decompression is a safe and effective method in the hands of experienced neurosurgeons, there are occasional complications. Ipsilateral deafness occurs in 0.5-1% of patients and there is a surgical mortality of approximately 0.2 %.
Effect occurring only after several days or weeks. However, the methods is accompanied with a high rate of relapses, so that after five years, only about half of the patients remains pain free. So far, few reports on repeat radiosurgery for trigeminal neuralgia are available. Some suggest that by an additional dose of about 20 Gy, secondary improvement can be achieved in some 50%.

Percutaneous Procedures
The percutaneous procedures are ablative procedures, comparable as radiosurgery. However, the target is within the trigeminal ganglion and not at the brainstem as with radiosurgery. With thermocoagulation, the trigeminal ganglion is thermally damaged and with glycerol infiltration chemically (3,8).

A special cannula is inserted under local anesthesia on the side of the corner of the mouth and guided into the foramen ovale under fluoroscopic control. The nerve is then heated with radio-frequency probe to a temperature of 70-85°C for a few minutes, or 0.3-0.4 ml of pure glycerol is injected. The balloon compression method also has been enjoying a certain popularity over the last decade, wherein a 4-French Fogarty balloon catheter is inserted through the foramen ovale and inflated with $0.75 - 1$ ml of contrast medium for a few minutes (5).

Thermocoagulation and glycerol infiltration have been used for over 20 years. Both methods achieve initial pain relief in 80-90%, but recurrence after some years is common, as with radiosurgery. A substantial sensory deficit occurs in about half of the patients, which is described in 10-15% as disturbing. Severe discomfort, so called anesthesia dolorosa occurs with similar frequency after thermocoagulation and glycerol injection (1.5 - 2%). After 5 years, some 50% of the patients still remain pain free.

The percutaneous interventions can all be repeated in the event of a recurrence. In general, however, the sensitive deficit increases after multiple interventions. The prospects for a repeated treatment are not as good as for the first procedure, but worthwhile improvement or complete relief can be expected in about 70% of repeat percutaneous interventions.

Trigeminal Neuralgia in Multiple Sclerosis and Atypical Trigeminal Neuralgia
Trigeminal neuralgia occurs in the course of about 2% of all patients with multiple sclerosis.

And it may result in the collapse of the balloon

The foramen ovale

Thermocoagulation

Glycerol injection

Secondary improvement can be achieved in some 50%.

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Trigeminal Neuralgia in Multiple Sclerosis and Atypical Trigeminal Neuralgia
Trigeminal neuralgia occurs in the course of about 2% of all patients with multiple sclerosis.
Traditionally, the destructive surgical procedures are recommended to these patients after exhaustion of drug treatment. Atypical trigeminal neuralgia includes facial pain that does not meet the aforementioned criteria of typical trigeminal neuralgia. In particular, there is in addition to paroxysmal attacks also constant pain and dysesthesia. The causes are diverse and include late development of an originally typical trigeminal neuralgia, postherpetic neuralgia, nerve damage, e.g. as a consequence of destructive procedures. Destructive methods are considered obsolete in these situations. Here, some success can be expected with an implanted neurostimulator (9).

Conclusions

The general acceptance of vascular compression as a cause of classical trigeminal neuralgia and the resulting possibility of curative treatment by microvascular decompression must be considered the most important recent progress with trigeminal neuralgia. Minimally invasive percutaneous procedures and Gamma Knife are still valid options for old or frail patients, since they can be performed without general anesthesia.

References

Treating Metastatic Melanoma in 2013

Introduction
The management of metastatic melanoma has yielded disappointing results until recent times. Some patients obtained a benefit from regional treatments, but the majority of them required systemic therapy that was largely ineffective. The advent of ipilimumab as the first immune check point control antibody and new knowledge of the molecular biology of melanoma has transformed this disease not longer conceived as one single tumour, but a constellation of related tumors having specific molecular characteristics. With the rapid development of specific kinase inhibitors the therapeutic landscape has dramatically changed. As new compounds enter clinical trials and eventually become widely available, decision trees will be required to use them correctly and which have to be adapted in short terms to integrate the newest developments. This article summarises evidence that may help in making clinical decisions and proposes an algorithm to use systemic treatments in 2013.

Key words: melanoma, advanced disease, BRAF inhibitor, MEK inhibitor, anti-CTLA4

Glossary: CTLA-4, cytotoxic T lymphocyte antigen 4 regulates immune functions; BRAF, serine-threonine kinase oncogene commonly mutated in melanoma; KIT, tyrosine kinase oncogene; NRAS, viral oncogene

Options and Outcome before the Era of New Drugs
The prognosis of patients with stage IV melanoma has remained unchanged for decades. A retrospective analysis published in 1983 showed a one-year survival rate of 40% for stage IVA and 11% for stage IVC disease [1]. In 2000, the Eastern Cooperative Oncology Group reported a median overall survival of 8-10 months in patients with soft-tissue or lung metastases and 6 months in those with visceral dissemination [2]. A systematic review of 41 randomised clinical trials revealed that combination regimens produced higher response rates, but at the cost of increased toxicity and with no benefit in overall sur-

سريرية وتفترض استخدام خوارزمية لاستعمال معالجات جهادية في عام 2013.

 المعالجة الإنتقالات
الورم الصباغي
في عام 2013

لقد حصلت معالجة الورم الصباغي المتمещة على نتائج غير مرضية حتى أوائل متأخرة. حصل بعض المرضى على نتائج موضعية مفيدة ولكن اتخاذ الأغلبية الى معالجة جهادية والتي كانت بشكل كبير غير مفيدة.

ipilimumab ان ظهور ايبمري ليمومب كخط أصداد دفاعي مناعي أولي وكذلك معرفة البيولوجي الجزيئية للورم الصباغي قد حولت المرضى من فكرة مرضى نوا ورم مفرد الى مجموعة من الأورام المتعددة لها ميزات جزيئية محددة. مع التطوير السريع لمت까지ت الكينات فقد تحول الخطوط العامة العلاجية بشكل جذري.

ولقد بخلت بعض هذه المركبات الجديدة الى الدراسات السريرية وبالتالي أصبحت مقبولا بشكل كبير وتحتاج استعمال مخطط شجرة القرارات من اجل استعمالهم بشكل قريب وتتحاج لتطبيقها الى وقت قصير وتندمج مع تطورات الأحداث.

يخلص هذا المقال الأبناء التي يمكن أن تساعد في اتخاذ القرارات السريرية معالجة دوائية مفيدة.
vival [3]. These trials had used single-agent chemotherapy, combination chemotherapy, interleukin-2 with or without interferon or combinations of chemotherapy and immuno-therapy. In view of the limited success of complex schemes, single-agent therapy with dacarbazine, which achieves responses in 7 to 15% of patients, was accepted as a reasonable standard of care in many institutions.

New Treatment Options since 2010

Immune Checkpoint Control using Anti-CTLA4 Antibodies
Ipilimumab is a fully humanised monoclonal antibody directed to CTLA-4 demonstrating that immune check point control is an effective cancer treatment option. Although overall response rates are low some long-term survival in some patients has been observed [4]. Furthermore 2 independ-

Fig. 1: The BRAF-MEK Pathway. Inappropriate activation of growth factor receptors (e.g., KIT) or mutations of the BRAF gene can lead to constant activation of MEK 1 or 2, with resultant effects on cells: increased proliferation, survival, and propensity for invasion.
Yervoy® has been approved on these results, ipilimumab been alive in the long term. Based on these results, ipilimumab showed little benefit in overall response rate or progression-free survival a survival plateau appeared after two years of follow-up, with 20% of patients remaining alive in the long term. Based on these results, ipilimumab (Yervoy®) has been approved in the US, Australia and Europe.

Since the mode of action of ipilimumab is different than all other oncological drugs, standard criteria for the evaluation of therapy response might be not sufficient for evaluation of treatment benefit of patients treated with ipilimumab. Main issue of confusion is an initial lymphocyte infiltration in the tumour which may increase tumour size or lead to the radiological appearance of “new or enlarged” lesions in computed tomography images (pseudo-progression). Furthermore, ipilimumab is associated with a new toxicity profile of immune-related side effects, mostly cutaneous and gastrointestinal, which requiring specific education and training of treating clinicians. Other antibodies having influence on the immune checkpoint control and that enhance the activity of the immune system are under current clinical development including those targeting PD1 and PD1 ligand.

Specific Therapy in BRAF Mutated Melanoma
The activation of the MAP-RAS-RAF signalling pathway is believed the critical pathway in melanoma development (Fig 1). Approximately 40% of melanomas present mutations in BRAF, usually V600E and less commonly V600K mutations or others. This has allowed the development of specific kinase inhibitors.

BRAF Inhibitors
Vemurafenib and Dabrafenib are selective BRAF inhibitors that target the V600 mutant forms of the BRAF. The drug is active only in tumours harboring the V600E mutant form of the BRAF. Vemurafenib and Dabrafenib have shown some activity in patients with BRAF V600E mutant melanomas, with an overall response rate of up to 15-20%.

Primary melanoma
Regression of lung metastases upon treatment with ipilimumab

Regression of lymph node mets upon ipilimumab treatment

Baseline
2012-07-03

Follow-up 1
2012-09-24

Regression of lung metastases within 12 weeks upon ipilimumab treatment

Regression of lymph node mets upon ipilimumab treatment
MEK Inhibitors

MEK is a downstream target of the BRAF pathway, which is depicted in Figure 1. A specific MEK inhibitor, trametinib, was recently tested in a phase III study, in comparison to chemotherapy (either dacarbazine or paclitaxel), in melanoma patients bearing a BRAF mutation. The results showed that trametinib is a first-in-class MEK inhibitor that conferred significant improvement in progression-free survival and overall survival, compared to either chemotherapeutic modality [9].

Combinations of Specific Inhibitors

Considerable effort is being dedicated to study the resistance to BRAF inhibitors and a number of mechanisms have been proposed. For instance, preclinical models indicate the importance of MEK dependency in BRAF-mutant melanoma [6].

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Melanoma and suggest that a combination of BRAF and MEK inhibitors could prevent the emergence of resistance. A phase II study of the BRAF inhibitor dabrafenib and the MEK inhibitor trametinib has shown encouraging activity with lower than expected toxicity [10]. Currently various registration studies are underway to proof the benefit of a combination of BRAF and MEK inhibitors over the monotherapy alone.

Major limitation of those targeted treatment approaches are the development of drug resistance. At this time, the best strategy to prevent or overcome resistance to BRAF inhibitors remains unknown and will be the aim of future clinical trials.

KIT Inhibitors
Approximately 15% of mucosal (with an especially high mutation rate in vulvovaginal melanomas; [11]) and 23% of acral melanomas have a mutation or amplification in KIT [12], which could allow therapy with specific inhibitors. Clinical trials utilizing imatinib or nilotinib show evidence of activity although treatment benefit is more heterogeneous (13).

Classical Chemotherapy and Other Compounds
Twenty per cent of melanomas harbour mutations in N-RAS, whereas uveal melanomas typically have mutations in GNAQ or GNA11, and other melanomas yet show a variety of other mutations (PI3K pathway, MITF, CDKs, etc.). Although MEK inhibitors could play a role in some of these uncommon subgroups of melanoma, specific inhibitors have not been developed, mainly because those mutations are less amenable to targeted therapy than BRAF or KIT. Further basic

وتجري حاليا عدة دراسات تسجيلية لاستخدام مثبطات MEK ومعنا مثبطات BRAF مع دواء واحد من استعمال العلاج الوحيد.

وتعتبر المقاومة الدوائية في المحدد الكبير لاستعمال هذه الطرق العلاجية. وفي هذه الأثناء فإن أفضل استراتيجية لمنع أو التغلب على المقاومة لمثبطات KIT تبقى غير معروفة وهي الهدف من الدراسات المستقبلية من دراسات KIT مثبطات 15% تقريبا من الأورام المخاطية.
research and multi-institutional cooperation will be critical in the future management of these subgroups. On the other hand, chemotherapy has traditionally been associated with poor overall results, but some patients clearly benefit from this approach. For this reason, chemotherapy will still have a place as rescue strategy in second or third line and in patients with non-mutated melanoma.

**Treatment Strategy in 2013**

As therapy for advanced melanoma becomes more complex, it is important to delineate treatment algorithms. Registration labels and drug availability will drive the sequence. At this time in early 2013, ipilimumab and vemurafenib have been approved by regulatory agencies, although cost constraints may limit access in some countries. Other new drugs and combination options mentioned above remain experimental. Considering the high response rate associated with vemurafenib, tumour genotyping is the first logical step. BRAF mutation should be searched for in all patients with advanced melanoma. Acral and mucosal melanomas should also be tested for mutations in BRAF and KIT. High-sensitive and quality controlled test assays are mandatory. Since RAS-mutated melanoma cases should be
Vemurafenib is the preferred option in patients with BRAF-mutated melanoma. However, ipilimumab could be considered in low-risk patients, i.e., those with low tumour burden and excellent performance status. Some of these patients could become long-term survivors, whereas the remaining would receive vemurafenib upon progression with ipilimumab. As ipilimumab requires time to produce an effective response, patients with short life expectancy could be better served with other options.

Imatinib or another KIT inhibitor is indicated if a KIT mutation is detected, although evidence in this regard is less consistent than in the case of vemurafenib and dabrafenib for BRAF-mutant melanoma. Ongoing studies will determine which KIT mutations are most amenable to treatment with this kind of inhibitors.

Patients progressing on vemurafenib, dabrafenib or a KIT inhibitor could receive ipilimumab or chemotherapy, depending on performance status and drug availability. Ipilimumab should also be considered as first line therapy whenever a targetable mutation is not detected in the tumour.

The importance of clinical trials cannot be overemphasized. The possibility to refer patients for clinical investigation should be considered at any stage of the patient's evolution. The treatment algorithm should be subjected to changes as new alternatives demonstrate efficacy for specific subgroups. For instance, the combination of BRAF and MEK inhibitors might be soon considered first-line for BRAF-mutated melanomas. In the future, specific drugs could be developed to treat melanoma with other mutations, in which the detection of these mutations should become standard of practice. Registration studies for melanoma bearing NRAS mutations are currently ongoing. Likewise, if markers predicting response to ipilimumab or anti-CD1 antibodies are finally found, they should be incorporated to the pathological workup.

Conclusions

In 2013, therapy for advanced melanoma is determined by the mutational status of the tumour. Selective BRAF-inhibitors such as vemurafenib and dabrafenib are the most referred to clinical trial centers offering treatment with MEK inhibitors, RAS mutation status should be ascertained in wild-type BRAF melanoma. The diagnosis of these patients could receive ipilimumab or chemotherapy, depending on performance status and drug availability. Ipilimumab should also be considered as first line therapy whenever a targetable mutation is not detected in the tumour.

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active agent in BRAF-mutant melanoma, whereas a KIT inhibitor could be considered in tumours with a mutation in KIT. Ipilimumab should be considered as first line for patients with no target mutations or as second line in any patients. Chemotherapy may have a role as salvage therapy in second or third line.

References
7. Hauschild A, Grob JJ, Demidov LV et al. Phase II, randomized, open-label, multicenter trial (BREAK-3) comparing the BRAF kinase inhibitor dabrafenib (GSK2118436) with dacarbazine (DTIC) in patients with BRAFV600E-mutated melanoma Dabrafenib in BRAF-mutated metastatic melanoma: a multicentre, open-label, phase 3 randomised controlled trial. Lancet Oncol 2012; Published online June 25, 2012 http://dx.doi.org/10.1016/S1470-2045(12)70431-X.
13. Carvajal RD, Antonescu CR, Wolchok JD et al. KIT as a therapeutic target in melanoma, whereas a KIT inhibitor could be considered in tumours with a mutation in KIT. Ipilimumab should be considered as first line for patients with no target mutations or as second line in any patients. Chemotherapy may have a role as salvage therapy in second or third line.

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Novel Methylene Blue Injection Directly into the Inferior Thyroid Artery (ITA) to Identify Parathyroid Gland During Thyroid and Parathyroid Surgery

Early Clinical Experiences in Daily Surgical Practice by Means of a Prospective Unicenter Observational Study

Abstract

Objectives (background): Based on the increasing number of clinical observations, which suggest a possible unfavorable neurologic outcome after traditional intravenous injection of methylene blue (MB) in several cases in the setting of (para)-thyroid surgery, the aim of this study was to investigate feasibility, success rate and accuracy as well as short- to mid-term outcome of a simple but novel technique (intraarterial i.a. administration of methylene blue).

Methods: Prospective unicenter observational study to assess surgical treatment quality in daily clinical practice at Alkadhimy Teaching Hospital, Baghdad (Irak) between 2007 and 2008.

Results: Thirty-five patients with surgically indicated thyroidal and parathyroidal diseases (n=28 [80%]) with age ranging from 28-65 years, who had undergone thyroid / parathyroid surgery at the Alkadhimy Teaching Hospital in Baghdad, were enrolled. One mL of methylene blue (final concentration, 0.1%) was administered into the inferior thyroid artery (ITA) intraoperatively. Thus, in thyroid cases, 44 out of 50 parathyroid glands were distinctly stained by the dye (88%). In parathyroidal disease, 16 out of 18 (88.8%) were tacked the dye, which can be considered an excellent and satisfactory result in the same range as reported in the literature, with an obviously low complication potential.

Conclusion: The presented technique can be recommended as a novel sufficient method, which can be considered a feasible and safe alternative in identifying efficaciously parathyroid glands for the endocrine surgeon as found in this pilot study on the novel i.a. methylene blue application mode into ITA. However, it needs further and continuing systematic evaluation in a greater number of patients to assess more appropriately short- to mid-term outcome aspects.

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Introduction
There is a great anatomic variety with regard to the local site as well as their numbers and incidence of parathyroids as has been reported by numerous authors. For instance, the number may vary from 1-12 but the regular number is 4 (87%) in the majority of cases: 2 at the superior and 2 at the inferior position, i.e., 2 pairs per person (in relation to the thyroideal gland). However, there may be 3 glands (6%), 5 glands (0.2%) and even 6 glands (0.6%) [1]. The parathyroid glands are usually visible only in 50% of cases. The middle third of the posterior border of thyroideal gland lodge the majority of these glands (60-65%) [2]. The average weight of a parathyroid gland is approximately 35 mg. The combined weight of the two superior and two inferior glands is therefore approximately 140 mg. Anatomically, the superior parathyroids can be mostly found at a site, which has developed from the 4th branchial arch, which is the same origin for the thyroid. Usually, the superior parathyroids are found within one cm from the cricoarytenoid joint at the posterior surface of the upper pole of the thyroid gland. In contrast, there is a great variety in the locations of the inferior parathyroids as they develop from the 3rd branchial arch, the same as for the thyroideal gland. However, there may be 3 glands (6%), 5 glands (0.2%) and even 6 glands (0.6%) [1]. The parathyroid glands are usually visible only in 50% of cases. The middle third of the posterior border of thyroideal gland lodge the majority of these glands (60-65%) [2].

Since the location of the parathyroid glands is quite variable, the surgical approach must be based on a competent knowledge of the embryological development of the parathyroids and their derived most common locations. As already stated, the superior parathyroid glands are less variable in anatomic site, with approximately 75% being located either crico- or juxtathyroidally.

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Fig. 1: Scheme on the locations and main blood supply of parathyroids.
In the majority of cases, the ITA supply to the parathyroids. In one percent, however, can be found either retroesophageally or retropharyngeally. The inferior parathyroid glands are more variable; approximately 40 % are located in the tissue immediately adjacent to the lower pole of the thyroid (both anteriorly and posteriorly) and another 40 % are located in the tongue of thymic tissue [3].

Fifteen percent will be located juxathyroidally, approximately 1 % are located in the mediastinum, and 2 % are ectopic, at any location along the migrational path from the base of tongue to the lower neck. For superior and inferior parathyroids, approximately 2 - 5 % of glands will be located within intrathyroidal tissue [3].

The glands have a rich blood supply originating from the natural anastomosis between superior and inferior thyroidal arteries. However, their direct main blood supply comes from the inferior thyroid artery (ITA), and there is a definite fascial compartment. Identifying and respecting this fascial compartment will save the blood supply to the parathyroids. In the majority of cases, the ITA contributes minimally to the arterial perfusion of the thyroid gland since most of the blood supply goes to the parathyroids. Avoiding surgical insult due to too aggressive handling or preparation or devascularising the parathyroid gland is of utmost importance in thyroid surgery, which recommends basically a superior-to-inferior dissection technique. Based on the increasing number of clinical observations, which suggest a possible unfavorable neurologic outcome after traditional systemic i.v. methylene blue (MB) infusion in the setting of parathyroid surgery, the aim of this study was to investigate feasibility, success rate and accuracy as well as short-term outcome of a simple but novel technique compared with the conventional approach, namely the application of methylene blue, by injecting intraoperatively 1 mL of it (final concentration, 0.1 %) directly into the gland and the tongue. And in this case, the MB injection can be as simple as direct injection of 0.1 % MB into the gland(s) near the thyroideum. The glands will be located within the thyroideum [3].

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into the ITA in order to
i) reliably identify the parathyroid glands during thyroid and parathyroid surgery [Fig. 1] but
ii) limit or reduce significantly the complication potential of the conventional approach.

Patients and Methods
During a defined time period, all consecutive patients with an indication for thyroid and parathyroid surgery admitted to AlKadhymia Teaching Hospital in Baghdad (Irak) because of various thyroid and parathyroid diseases (inclusion criteria) were enrolled in this prospective uncenter observational clinical study according to the study aim; patient- as well as intervention-related characteristics were documented in a computer-based registry.

The primary endpoint was the feasibility of the novel method by identification rate (in particular, success rate and accuracy) of the parathyroids further characterized by the number of parathyroids per patients in using the novel direct injection of methylene blue into the ITA. The secondary endpoint was outcome characterized by short-term follow-up (postoperative return of the serum calcium level to normal) as well as perioperative morbidity and mortality.

The preoperative approach and the intraoperative measures were, in brief [Figs. 2-4]: Patients were referred from the department of endocrinology after all the relevant diagnostic investigations had been accomplished and the patients had been prepared for surgery as indicated including informed consent form in each case. General anesthesia in reverse Trendelenburg’s position with the neck slightly extended was used in all cases. The standard neck incision is made measuring about 8-12 cm in length at the lower part of the central neck [Fig. 2]. After opening the pretracheal fascia in the midline and mobilisation of the sternothyroid muscle, the thyroid gland is mobilised to allow searching for the four parathyroid glands, which reside moderately deep in the neck behind the thyroid. In all cases, ITA was subsequently identified preserving recurrent laryngeal nerve of the cervical curve. In this position, the novel instrument was introduced in the ITA. The secondary endpoint was outcome characterized by short-term follow-up (postoperative return of the serum calcium level to normal) as well as perioperative morbidity, including hospital stay.

This approach allows for the precise identification of the parathyroid glands and avoids the complications associated with the conventional approach.

Conclusions
The feasibility of the novel method was demonstrated in a series of patients with parathyroid adenoma. The success rate was 100% in all cases, with no complications reported. The method is safe and effective and can be used as an alternative to the conventional approach.

The results of this study suggest that the novel method is a viable alternative to the conventional approach and should be further evaluated in larger studies.
In case of parathyroid left in situ. The other glands for parathyroid adenoma, half was kept in situ.

In case of hyperplasia of there. In particular:

- In case of parathyroid carcinoma, we removed the gland with ipsilateral thyroid lobectomy.

All removed parathyroid glands, which have dark purple colour, are casually visible under the fascial layer; they were subjected to histopathologic investigation. In subjects with thyroid disease, FNAC confirmed the clinically diagnosed parathyroid gland. The patients in whom a nodule was not proved to be part of parathyroid gland were excluded from the study. Because of possible alterations of serum calcium levels in the postoperative observation period, serum calcium was measured every 6 to 8 hours during the first few days [4]. Potential symptomatic hypocalcemia was prevented by initiating calcium tablet supplementation for 1-2 weeks.

The study was undertaken according to the guidelines of Helsinki.

In case of hyperparathyroidism, the procedure is repeated at the contralateral side in order to identify the glands there. In particular:

- In case of hyperplasia of the parathyroidial glands, three and a half glands were removed, the remaining half was kept in situ.

- For parathyroid adenoma, only the pathologic adenoma was removed mostly associated with one of the glands. The other glands were investigated to exclude multiple adenomas; then, these glands were also left in situ.

- In case of parathyroid gland, which runs near the artery, freed from adhesions to the soft connective tissue and slightly fixed with loose loops of absorbable suture material. After this, 1 mL of methylene blue (vial of 50 mg were diluted in 5 mL (resulting concentration of the stock, 1 %) was administered (after further dilution 10 times using 0.9 % of saline resulting in a final concentration of 0.1 %) using an 1-mL (“insulin”) syringe and a (27G)Fr.-curved injection needle or (22G)Fr.-cannula (depending on the diameter of the artery) into the ITA apart from the thyroid gland (to avoid injury to the recurrent laryngeal nerve). The dye was intravenously administered (after further dilution 10 times using 0.9 % of saline resulting in a final concentration of 0.1 %) using an 1-mL (“insulin”) syringe and a (27G)Fr.-curved injection needle or (22G)Fr.-cannula (depending on the diameter of the artery) into the ITA apart from the thyroid gland (to avoid injury to the recurrent laryngeal nerve). The dye was intravenously administered (after further dilution 10 times using 0.9 % of saline resulting in a final concentration of 0.1 %) using an 1-mL (“insulin”) syringe and a (27G)Fr.-curved injection needle or (22G)Fr.-cannula (depending on the diameter of the artery) into the ITA apart from the thyroid gland (to avoid injury to the recurrent laryngeal nerve). The dye was intravenously
of the Declaration of Helsinki for Biomedical Research from 1964 and the standards of the Institutional Review Board as appropriate. Informed consent for surgical intervention was obtained from each patient as appropriate.

Results
From 2007 - 2008, in total 35 (sex ratio: females, n=28 [80 %]; males, n=7 [20 %]) with age ranging from 28 - 65 years were diagnosed with various thyroid and parathyroid diseases and were subsequently admitted to the AlKadhymia Teaching Hospital in Baghdad (Iraq) for surgery. Out of these cases, 24 patients (68.5 %) showed multinodular goitre, 3 (8.5 %) diffuse hyperthyroidism, 3 (8.5 %) parathyroid hyperplasia, 1 (2.85 %) single parathyroid adenoma, 2 (5.7 %) thyroid adenoma, and thyroid tumour as well as parathyroid carcinoma was found in one patient each (2.85 %), respectively [Table 1].

Out of 68 detectable parathyroid glands in total, 18 glands were detected in parathyroid cases (n=5) with an average rate of 3.6 per case, whereas 50 glands were detected in thyroid cases (n=30) with an average rate of 1.7 per case [Table 2]. Sixty (88.2 %) glands were located at an orthotopic position and further 8 (11.8 %) near the carotid sheath. In patients with pathology of the thyroid gland (n=30), 44 out of 50 glands were clearly stained by the dye (success rate, 88 %) [Table 3]. Four glands (8 %) were not tacking the dye due to technical failure as it happened severely in one case, thus, ITA could not be identified using this method. The spectrum of surgical interventions ranged from simple lobectomy to near total thyroidecтомy with preservation of the(both) recurrent laryngeal nerves(s) and parathyroid glands. In cases with diseases of the parathyroidal gland (n=5), 16 out of 18 (success rate, 88.8 %) were tacking the dye. Two glands (11.2 %) did not resorb the dye, which were located near the carotid sheath lower down in the neck.

All patients recovered well from anesthesia without any complications. Informed consent for surgery was obtained from each patient as appropriate.

Fig. 4b: Parathyroid gland and recurrent laryngeal nerve
complication. Postoperative hospital stay with an average of 3.5 (range, 2-5) days was uneventful in almost each case. Interestingly, there was only one case with a postoperative symptomatic hypocalcemia who needed additional i.v. administration of calcium gluconate (100 mL of 10 % calcium gluconate over 4 hours) (perioperative morbidity, 2.9 % [n = 1/35]). However, there was no allergic reaction or mental disorientation with regard to methylene blue application, neither a specific complication such as postoperative bleeding or wound infection, general complication such as urinary and pulmonary infection nor even postoperative death (hospital mortality, 0).

Discussion
Due to small size, variable appearance and anatomic position, (partially extended) intraoperative search for the parathyroid gland occurs not rarely, can frustrate the surgeon and can significantly prolong the operating time. Hypoparathyroidism is a well recognised complication of thyroid surgery and recurrent hypercalcemia is also a well known sequela of parathyroid surgery for primary hyperparathyroidism. Preoperative staining of the parathyroid glands has been shown to help to overcome the problem.

Dudley in 1971 introduced the use of methylene blue and considered this a reasonable and safe approach [5]. In 1975, Gordon and co-workers advocated also the use of methylene blue for this purpose [6,7]. Cox and colleagues in 1979 reported on the application mode and efficacy of this technique [8]. In 1986, Bland and associates reviewed the technique and reported a significant reduction in operating time due to ease of locating the glands. During the following few years, the role of methylene blue faded especially after the observation of neurological side effect that had been reported after i.v. infusion in the literature [9], e.g., mental toxicity by traditional methylene blue application for search of parathyroids and following parathyroidectomy. Martindale et al. [10] have reported a patient who had rotational nystagmus and dilated pupils unreactive to light in the recovery

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Thirty minutes later, the patient displayed rigid, jerky movements of all four limbs and remained very agitated with fluctuating Glasgow Coma Scale (GCS) of 7–10 for the subsequent 2 h. Arterial blood gases demonstrated respiratory acidosis and the patient needed to be re-intubated. The speech and the neurological status returned to normal within 2 days. Bach et al. [11] have described that their patient had marked aphasia in the recovery. Within the next few hours, the aphasia improved, but the patient’s speech remained slow and he was not oriented to time and place. The patient remained calm and pleasant throughout his hospital course. His mentation returned to normal after 2 days. The risk appears to be dose-dependent. Khan et al. have reported on their patient’s speech remained aphasic and altered mental status during the early postoperative course secondary to traditional infusion of methylene blue (5 mg/kg) according to 370 mg in 500 mL of glucose 5 % started 1 h before surgery and continued during surgery [12]. Such risk has not occurred in our series due to low concentration and volume of methylene blue used and the advantage that i.a. administration of methylene blue led to no systemic distribution of the dye with possible unfavorable consequences. Methylene blue has been safely used intraarterially in identification of endocrine pancreatic tumours [13] or i.a. methylene blue was injected into the inferior mesenteric artery as a novel method to improve lymph node (LN) detection [14]. In the presented study, 60 out of 68 detectable glands (88.2 %) were found by the novel i.a. methylene blue application mode, which can be considered an excellent and satisfactory result in the same range as obtained by Bland (90 %) [15] and Wheeler (86 %) [16].

The open question is still the appropriate concentration of methylene blue since, if it is too concentrated, it makes the thyroid gland and the perithyroidal connective tissue dark blue with no reasonable chance to be able for further careful preparation and adequate differentiation of various tissues and anatomical structures. Occasionally, thyroid gland assimilates the dye, in particular, thyroid cyst can incorporate it but this can be distinguished from the parathyroid gland by macroscopic features seen intraoperatively.

Sometimes, cannulation of the ITA can be difficult since the injection site is usually at the in and approaches the ascending aorta with the sac of the aortic arch. However, this procedure can be performed at the iliac artery or at the aortic wall. The advantage of this technique is that it is less invasive and safer than the traditional approach.

The distribution of the methylene blue can be affected by the concentration and volume used. A low concentration and volume can limit the systemic distribution, whereas a high concentration and volume can lead to serious complications.

Table 1: Thyroid and parathyroid disease types (nTotal=35)

<table>
<thead>
<tr>
<th>Characteristics of tissue</th>
<th>Multi-nodular</th>
<th>Diffuse hyperplasia</th>
<th>Adenoma</th>
<th>Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid</td>
<td>24</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Parathyroid</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
in the deepest part of the operative situs, which requires patience and skills. Taken together, the use of methylene blue for injection into the ITA to identify parathyroid glands requires an experienced endocrine surgeon with expertise in both thyroid and parathyroid anatomy and surgery. However, there are further limitations, e.g., in one case, the ITA could not be identified at all, or, in another case, the superior thyroid glands are not supplied by blood from the ITA, which i) has not become obvious in the case presented here, most likely due to rich natural anastomoses and a well-developed net of arteries and collaterals, and ii) can only be observed in larger series of patients with various peculiarities of supplementary arteries.

Conclusions
In developing countries, it is not always possible to use cost-intensive tools in the majority of cases. Therefore, the role of methylene blue should be considered an appropriate alternative technique, which is safe and feasible, in particular, i) with regard to tolerability and complication rate, ii) to simplify the search for and reliably identify the parathyroid glands intraoperatively, and iii) to achieve very likely a sufficient limitation in operating time and costs, which should be addressed in a subsequent study in a greater number of patients.

Table 2: Detectable parathyroid glands (nTotal=68)

<table>
<thead>
<tr>
<th>Operation</th>
<th>Total cases</th>
<th>Detected glands</th>
<th>Average per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid</td>
<td>30</td>
<td>50</td>
<td>1.6</td>
</tr>
<tr>
<td>Parathyroid</td>
<td>5</td>
<td>18</td>
<td>3.6</td>
</tr>
</tbody>
</table>

In conclusion, the presented technique can be recommended as a novel sufficient alternative method in identifying parathyroid glands for the endocrine surgeon, which can have a beneficial effect on the detection rate and can quicken the search for the parathyroid glands. Further systematic evaluation is needed to emphasize the favorable benefits and elucidate disadvantageous limitations for a reasonable and suitable use in an appropriate group of (possibly only selected) patients.
Parathyroid Gland

References


Table 3: (Para-)Thyroid staining (nTotal=68)

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Stained</th>
<th>Not stained</th>
<th>In total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid</td>
<td>44</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>Parathyroid</td>
<td>16</td>
<td>2</td>
<td>18</td>
</tr>
</tbody>
</table>
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