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Pre-augmentation soft tissue expansion: an overview

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Abstract

Objectives: The aim of this study was to explore the development of soft tissue expanders, their different types and their potential applications prior to bone augmentation and implant placement.

Material and Methods: A review of pertinent literature was performed using PubMed to comprehend the dynamics of soft tissue expanders and determine the current position of their pre-augmentation applications.

Results: There is promising, albeit preliminary information regarding the benefits of pre-augmentation soft tissue expansion. Findings cannot be generalised due to relatively small sample size.

Conclusions: Further clinical trials with larger sample sizes and long-term follow-up are needed before soft tissue expanders can be confidently applied in everyday clinical practice.

Periodontal disease is one of the most common diseases of the oral cavity, and it is prevalent in about half of the American adults (Eke et al. 2012). Left untreated periodontal disease can progress and cause destruction of the attachment apparatus and loss of the supporting alveolar bone, eventually ending in tooth loss. In fact, periodontal disease is listed as the major cause of tooth loss in adults (Jenkins et al. 1988). Yet, dental caries also contributes to high incidence of edentulism (Copeland et al. 2004).

If there is no early replacement of lost teeth, bone resorption will start and progress, causing significant changes of both the horizontal and vertical dimension of the alveolar ridge (Liu & Kerns 2014). Most of these alterations occur within the first 3 months after extraction; Schropp et al. (2003) reported a loss of 50% of crestal width within these early stages. Current literature confirms that tooth extraction without replacement may result in a reduction of 40% of bone height and 60% of bone width within the course of 2–3 years after tooth loss (Ashman 2000).

In cases of severe bone resorption, vertical and/or horizontal bone augmentation procedures are mandatory prior to placement of implants to achieve adequate dimensions of the alveolar ridge, which in turn is necessary to accomplish successful outcomes of implant therapy, especially in anterior maxilla which is an area of high aesthetic priority.

Different techniques have been described for bone grafting: bone block and/or guided bone regeneration (GBR) are used for horizontal bone augmentation, with a good predictability and satisfactory final outcomes (McAllister & Haghighat 2007). Vertical bone augmentations are technique sensitive as well but even more challenging. Several surgical techniques can be applied, such as vertical GBR, onlay grafting, inlay grafting and distraction osteogenesis (Rocchietta et al. 2008; Esposito et al. 2009). Moreover, vertical bone augmentations are associated with high complication rates, mainly soft tissue dehiscences, which are the primary cause for bone graft exposures (Lundgren et al. 2008). As a negative consequence, such complication can lead to eventual partial or complete loss of the bone augmentation material. Wound dehiscences with subsequent bone graft exposure may occur in up to 20% of vertical bone augmentations (Jensen & Terheyden 2009; Kaner & Friedmann 2011). Similarly,

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Proussaefs & Lozada (2005) reported about 25% of bone graft exposures in patients who got vertical bone augmentation with autogenous bone blocks. This complication rate was even higher (50%) in a work published by Roccuzzo et al. (2007). In general, high incidence of bone graft exposures has been documented in the literature (Verhoeven et al. 1997; Chiapasco et al. 2004; Merli et al. 2007). Due to the aforementioned high complication rate, the use of short dental implants was suggested as an alternative to grafting procedures in atrophic areas (Esposito et al. 2011). This might be an acceptable option in the posterior area. However, in the zone of aesthetic priority, severe bone resorptions have to be compensated by augmentation procedures to achieve satisfactory aesthetic results.

As high complication rate has been observed with different vertical bone augmentation techniques, it can be extrapolated that such complications might not be associated with the applied augmentation technique per se, but rather with the execution and precision of the surgical procedure, mainly with management and manipulation of the soft tissues.

To ensure a successful final outcome of any surgical procedure, a tension-free (passive) primary closure of the soft tissues is important to preserve the vascularisation of the tissues (Cordaro et al. 2002) and to reduce the risk for subsequent post-surgical infections (Wang & Boyapati 2006a,b).

As soft tissues follow the underlying bony contour (Sonick & Hwang 2007), severe alveolar bone resorption in either the maxilla or the mandible is usually accompanied by a limited amount of soft tissues, which impairs a tension-free primary closure of the soft tissues. This might be even more compromising when large amount of bone-grafting materials are to be used (e.g. bone block grafts) in vertical and/or horizontal bone augmentation procedures.

As a consequence in an attempt to achieve complete and tension-free primary soft tissue closure over the grafted area, flap advancement is usually performed by mobilising the muco-periosteal flap by deep periosteal releasing incisions. This approach has been recommended following major bone-grafting procedures to achieve the aforementioned goals (Greenstein et al. 2009). Vertical releasing incisions negatively affect the perfusion of the muco-periosteal flap (Mormann & Ciancio 1977; Jivraj & Chee 2006; Esposito et al. 2007), and because preservation of sufficient blood flow is essential for the nutrition of the soft tissues, a decrease in flap vascularisation increases the risk of soft tissue dehiscence (Nakayama et al. 1982). Moreover, periosteal releasing incisions compromise the integrity of the periosteum overlying the bone graft, which results in diminished blood supply to the bone graft (Abrahamsson et al. 2010), less new bone formation and poor bone remodelling activity (Zhang et al. 2008). The periosteum is a fundamental source of osteoblasts and their precursor cells (Allen et al. 2004), and hence, presence of vital periosteal progenitor cells on the surface of bone grafts accelerates bone healing (Xie et al. 2007).

Moreover, flap advancement may result in a reduction of the vestibule and a coronal displacement of the muco-gingival junction, which may compromise the final aesthetic result and impair cleansing around prostheses on implants (Jung et al. 2014).

When extensive flap advancements are required, even if flap passivity has been achieved with releasing incisions, the risk for wound dehiscences may increase with negative consequences for the underlying bone graft (Lundgren et al. 2008; Burkhardt & Lang 2010). Moreover, incomplete soft tissue coverage results in a limited contact with area between bone and flap, which in turn is necessary for re-vascularisation of the bone graft (Moghadam 2009) and which is important in the prevention of an accelerated resorption of the bone (Zerbo et al. 2003). It has been documented that flap tensions result in wound dehiscences, irrespective of flap thickness (Burkhardt & Lang 2010). In a clinical study on implant patients, wound dehiscences occurred in 40–100% of sites exposed to high flap tensions (Burkhardt & Lang 2010).

In general, flap mobilisation seems to increase the risk for soft tissue dehiscences and, as a consequence, to compromise the survival of the underlying bone graft. Attempts to minimise the risk of post-surgical soft tissue dehiscence have been made by utilising extra-oral approaches in bone augmentation. Placement of bone grafts through extra-oral incision was encouraged to avoid the risk of intra-oral incision breakdown (Bell et al. 2002). This approach was also adopted to expose the facial blood vessels for anastomoses with free fibula flaps (segment of bone with vascularised pedicle), to compensate for the poor vascularisation of soft tissues associated with atrophy (Rohner et al. 2002; De Santis et al. 2004; Chiapasco et al. 2011). However, these methods are invasive as they involve patient hospitalisation and an increase in morbidity rate.

Notably, a considerable amount of bone graft volume resorbs during the post-operative healing phase and as a part of the remodelling process regardless of other factors (Cordaro et al. 2002; McAllister & Haghighat 2007). A compromised mucosal vascularisation and lack of tissue integrity will accelerate bone resorption, beyond the commonly seen remodelling activity (Lundgren et al. 2008; Rothamel et al. 2009). Hence, to prevent such unfavourable results, improvement of the quantity and quality of soft tissues overlying bone grafts must be taken into consideration (Kaner & Friedmann 2011).

An increase in soft tissue volume overlying bone is well documented in distraction osteogenesis, which induces an expansion of both bone and covering soft tissues (Rocchietta et al. 2008; Esposito et al. 2009). However, bone distraction is a complex and technically demanding procedure. It requires a special device that must be applied properly to avoid serious complications (Uckan et al. 2002).

Alternatively, less invasive methods to create a surplus of soft tissues, and therefore reduce the risk for mucosal dehiscences, have been investigated: periosteal distraction (Schmidt et al. 2002; Kessler et al. 2007; Sencimen et al. 2007; Oda et al. 2009; Tudor et al. 2010) and tissue engineered periosteum (Schönmeyr et al. 2009; Warnke et al. 2009). In spite of the promising results, these methods are still experimental and have been tested only in animal experiments. Further investigations are obligatory to validate the eligibility for their clinical applications.

Soft tissue expansion

Soft tissue expanders have been introduced in implant surgery, as pre-augmentation devices, to avoid the complications associated with bone-grafting procedures (Kaner & Friedmann 2011; Mertens et al. 2015). The concept of soft tissue expansion is based on the biological properties of various soft tissues, such as skin or mucous membranes, to react to applied mechanical forces by true tissue growth (cell proliferation) (Neumann 1957). This phenomenon can be observed in abdominal skin during pregnancy, obesity, muscle growth or lip and neck expansion as a part of African traditions (Johnson et al. 1993). Soft tissue expanders have the capability to enlarge soft tissue volumes without altering its thicknesses and to generate tissues with appropriate colour match and texture similar to that of the original tissues (Fang et al. 2013). One of the clinical indica-

tions of such technique is the preoperative expansion of the oral mucosa when large bone augmentations are planned. An overamount of soft tissues might reduce the need for periosteal incisions and guarantee a passive flap closure covering the bone graft. Further, intra-oral applications of soft tissue expanders include the repair of lip and/or palate clefts.

The use of soft tissue expanders became popular in the field of plastic surgery since 1976 (Uijlenbroek et al., 2011). The applications are well established for many indications, ranging from correction of skin burn after burn wounds, scars, alopecia, congenital nevi to post-mastectomy breast re-construction (Berge et al. 2001; Ronert et al. 2004; Obdeijn et al. 2009; Chummun et al. 2010). Recently, the "concept" of soft tissue expansion has been introduced in orthopaedics. In a clinical report, the successful application of an "external" soft tissue expander to achieve skin closure in open fractures was described (Formby et al. 2013).

History and types of soft tissue expanders

Soft tissue expanders were first developed by Neumann in 1957; who applied a subcutaneous rubber balloon to expand skin tissues in order to repair an ear defect. Nonetheless, it was not until the early 1980s when the real interest in soft tissue expanders re-surfaced, particularly in breast reconstruction (Radovan 1982) and treatment of burns (Argenta et al. 1983). The expanders used in these early stages were made of silicone rubber, with an external valve penetrating the skin for manual inflation by serial injections, as illustrated in Fig. 1.

The amount of soft tissue gain with conventional expanders has been reported to be dependent on the type of expanded tissues and the shape of the expanders (Brobmann & Huber 1985; van Rappard et al. 1988). It was observed that tissue gain was more pronounced with rectangular and crescentic forms compared with round-based expanders (Johnson et al. 1993).

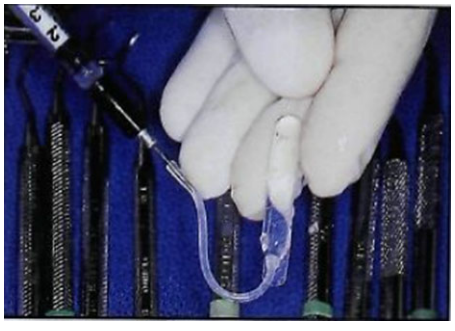

Fig. 1. Conventional expander with an external port for serial injections and manual inflation. *Courtesy of:* Zeiter et al. (1998).

Despite the positive results with conventional expanders, they have several disadvantages, such as repetitive inflations, which may increase the treatment time up to several months. The intermittent modality of external inflations creates pressure peaks with a reduction in the tissue vascularity (Pietila 1990), which in turn may cause an expander perforation through the soft tissues (Wiese 1993). A lack of perfusion caused by pressure peaks reduces the local oxygen partial pressure of the soft tissues and therefore increases the risk for expansion failures (Berge et al. 2001). Additionally, serial injections increase the costs of treatment and morbidity of the patients as well as the risks for adverse effects by repeated punctures. Despite these drawbacks, conventional soft tissue expanders are still used in plastic surgical procedures. Due to the above-mentioned shortcomings, the use of conventional expanders is limited in cranio-facial defects (van Damme et al. 1992).

To overcome the disadvantages of conventional soft tissue expanders, Austad & Rose (1982) developed a self-inflating osmotic soft tissue expander, without an external port and no need for repetitive inflations. The new type of expander was based on a semi-permeable silicone membrane which contained hypertonic sodium chloride solution. The osmotic gradient allowed a continuous inflow of body fluids into the expander. As a consequence, the expander volume increased with concomitant soft tissue growth. As a negative effect, leaks occurred from the shell of the expander to the surrounding tissues resulting in tissue necrosis. These complications made the device inappropriate for clinical application.

To overcome this major drawback, Wiese (1993) developed a novel self-inflating osmotically active soft tissue expander made of hydrogel.

It consists of both a polymer network (cross-linked hydrogel of co-polymers based on methyl methacrylate and N-vinyl-pyrrolidone) (Wiese 1993; Wiese et al. 1999, 2001) and a variable aqueous component (Refojo 1975). Since 1999, this hydrogel expander has been designed and manufactured under the name of Osmed® (Ilmenau, Germany), which is the first commercially available self-inflatable osmotic expander and has been FDA-approved since 2001.

The biomaterials used are the same like in contact lenses and offer a high biocompatibility without eliciting any toxic effects, adverse immune reactions, infections or any other systemic manifestations, and most importantly, they do not provoke any localised inflammatory reactions in the soft tissues (Wiese et al. 2001). Incorporation of methacrylate, in general, produces ionic hydrogels due to the presence of carboxyl moieties, which results in a greater osmotic potential and subsequent amplification of the swelling capability in comparison with non-ionic hydrogels (Wiese et al. 2001). Inclusion of "methyl" methacrylate, specifically, in osmotic hydrogel expanders results in an increased swelling ratio (Wiese 1993; Wiese et al. 1999, 2001) when compared to "hydroxyethyl" methacrylate (Downes et al. 1992).

The presence of cross-links renders the polymer network insoluble in aqueous media (Bell & Peppas 1996); thus, the expander has the ability to swell and retain large volumes produced by swelling and not dissolve in the aqueous media. In an effort to test different biomaterials, Varga et al. (2009) developed a hydrogel osmotic soft tissue expander made of either acrylamide (AAm), acrylic acid (AAc) or N-isopropylacrylamide (NIPAAm). Although NIPAAm hydrogels were proven to be the most appropriate biologically and mechanically for applications in plastic and reconstructive surgeries, these expanders were only tested *in vivo* and remain to be validated in clinical trials.

As osmotic expanders abolish the need for serial injections, they inflate continuously by osmotic gradients without the need for additional interventions. A constant expansion compared to an intermittent inflation results in the formation of new cells, tissue growth (van Rappard et al. 1988), and a greater amount of final tissue gain (Wee et al. 1992; Bennett & Hirt 1993; Bascom & Wax 2002).

Absence of an external filling port minimises the bulkiness of the expansion device (Swan et al. 2012), which facilitates the positioning of the expanders. With a starting volume of just 10% of the final volume, osmotic expanders are initially smaller in size than conventional expanders (Ronert et al. 2004). As a consequence, osmotic expanders require smaller incision for insertion (Chummun et al. 2010), which reduces surgical trauma (Figs 2 and 3). Miniaturised osmotic expanders have been successfully used in clinical ophthalmology (Schnittkowski et al. 2003) and opened new indications in paediatric surgery (Obdeijn et al. 2009).

There are two generations of Osmed® hydrogel soft tissue expanders. The first genera-

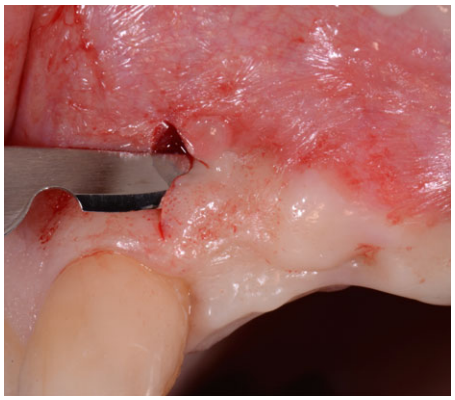

Fig. 2. Small incision is created for the insertion of osmotic soft tissue expander. "*Courtesy of:* Rasperini, G. University of Milan, Department of Biomedical, Surgical and Dental Sciences, Foundation IRCCS Ca' Granda Polyclinic, Milan, Italy".

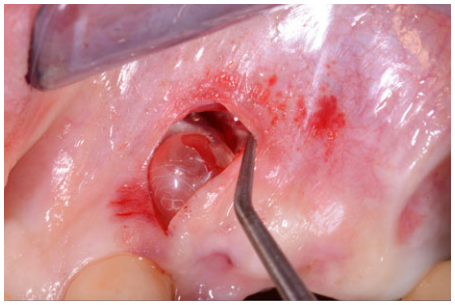

Fig. 3. Osmotic expander inserted through small incision. "*Courtesy of:* Rasperini, G. University of Milan, Department of Biomedical, Surgical and Dental Sciences, Foundation IRCCS Ca' Granda Polyclinic, Milan, Italy".

tion lacks a silicone envelope surrounding the surface of the hydrogel which results in extremely rapid expansion, in the early stages after insertion with consequent complications (Rees et al. 2008). Importantly, rapid inflation does not result in an actual increase in soft tissue volume because tissues need time to adapt (Uijlenbroek et al., 2011). Early studies showed that tissues might return to their pre-expansion status in the case of rapid expansion (Johnson et al. 1993).

To avoid such undesirable outcomes, a second generation of osmotic hydrogel soft tissue expanders, coated with silicone, have been introduced in 2001 (Ronert et al. 2004). Both generations are displayed in Fig. 4.

The perforations in the "impermeable" silicon shell allow the influx of surrounding fluids. The number of perforations controls the inflow rate which in turn limits the speed of expansion (Kaner & Friedmann 2011). Compared to the first generation, a less steep swelling curve of the second-generation expanders represents a continuous expander growth with less pressure peaks (Ronert et al. 2004; Anwander et al. 2007). In other words, inclusion of silicone coating adjusts the expansion speed overall, which gives more time for the newly formed tissues to adapt, more time for wound healing and results in greater amount of expanded tissue (Wee et al. 1992), and effective soft tissue generation (Wiese 1993; Wiese et al. 2001). Comparisons between osmotic expanders and conventional expanders are summarised in Table 1.

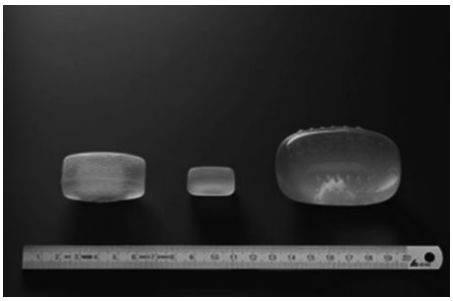

Fig. 4. Rectangle osmotic hydrogel expander: from left to right: un-swollen, without silicon shell, swollen. "*Courtesy of:* Osmed® GmbH (Ilmenau, Germany)".

In the following, we will refer to Osmed® expanders as they are the most widely applied commercially available expansion devices with sufficient evidence-based data.

Shapes, dimensions, expansion time and speed of osmotic expanders

Osmotic soft tissue expanders are available in different shapes with diverse "prior to insertion/post-insertion" dimensions to match their area of application. For example, round shape is mainly used in breast reconstruction, while rectangular shape is recommended for defect coverage after excision of large skin tumours and burns (Ronert et al. 2004). For intra-oral uses, hemispheric and cylindrical shapes are recommended by the manufacturer.

Table 1. **Comparison between conventional and osmotic soft tissue expanders**

Characteristic	Osmotic expanders	Conventional expanders
First development of "concept"	Austad & Rose (1982)	Neumann (1957)
Presence of an external portal	No	Yes
Size	Small size, needing small incisions for insertion	Bigger than osmotic expanders
Material	Hydrogel cross-linked co-polymers Lack of silicone coating in first generation Presence of silicone coating in second generation	Elastic silicone rubber
Mechanism of expansion	Spontaneously by osmotic forces from surrounding fluids	Manual inflation by serial injections through external portals, by either the clinician, patients, parents or guardians
Use in paediatric patients	Encouraged	Discouraged, due to injection-related pain
Time for expansion	Weeks or months	Weeks or months
Mode of expansion	Continuous Rapid with first generation Gradual and slow in second generation	Intermittent
Development of pressure peaks	Yes (first generation) No (second generation)	Yes
Complications	Minimal rate of complications (mainly with second generation) Chances for relapse with first generation	Infections, pain, ischaemia and perforation
Amount of soft tissue gain	Excellent amount due to constant & gradual pressure (second generation) Lack of actual tissue gain with first generation occasionally	Depends on the expanded host soft tissue and the shape of the expander
Cost	Lower cost	Higher cost because of the need of serial injections
Area of current applications	Craniofacial, intra-oral, ophthalmologic applications and plastic surgery	Limited uses in plastic surgery

"Pre-insertion/post-insertion" dimensions are accurately defined for each expander, which simplifies surgical planning.

Once inserted, osmotic expanders have the capability to expand ten times of their original volume (Chummun et al. 2010), within the time of approximately 6–8 weeks post-insertion (Obdeijn et al. 2009). Results from studies concluded that expanders can reach six times their original volume, 2 weeks after insertion (Abrahamsson et al. 2010).

This duration primarily depends on the anatomical location, size of the defect (Ronert et al. 2004) and the dimensions of the expander (Mertens et al. 2015). Expanders with bigger pre-insertion/post-insertion dimensions require more time to achieve their final size. Accordingly, the duration of expansion may vary from 10 days to 8 weeks (Ronert et al. 2004). Furthermore, the expansion speed that dictates the time frame to complete swelling depends on the shape of the expander.

Round expanders for breast reconstructions are left for approximately 4–6 months, as they are replaced later on by permanent implants.

As osmotic expanders have different shapes and dimensions, each model apparently has its own swelling curve. It is impossible to modify the swelling characteristics of a certain type of expander after insertion (Uijlenbroek et al., 2011), and therefore, the appropriate expander model should be chosen prior to surgical placement.

Intra-oral applications of soft tissue expanders

In cranio-facial surgery, the application of expanders was first described by Argenta & VanderKolk (1987). The use of soft tissue expanders prior to bone augmentation of the severely atrophic mandibular ridge has been encouraged by early reports (Lew et al. 1988, 1991; Wittkampf 1989; Schwartz & Relle 1990; Bahat & Handelsman 1991; Zeiter et al. 1998). However, conventional expanders in the shape of silicone balloons were applied in all these cases and they included few patients without long-term follow-up, in terms of stability or relapse of expanded soft tissues and outcomes of hard tissue procedures following expansion. Recently, osmotic hydrogel soft tissue expanders of the second generation have been investigated in intra-oral applications.

Uijlenbroek et al. (2011) tested osmotic soft tissue expanders in an animal study. To validate the effectiveness and efficiency of soft tissue expanders in various intra-oral applications, the researchers placed the expanders in the palatal mucosa of goats. As the palatal mucosa is very firm in these animals, the researchers hypothesised that a similar expansion would be successful in the oral cavity of humans. Expanders were implanted for 40 days, using either a "tunnel" approach or a "flap" approach. After swelling, the expanders had created a surplus of soft tissues with an excellent shape and no signs of inflammation. Histological analysis revealed no signs of bone resorption, despite the pressure exerted on bone, which is equal to the amount of pressure needed to expand the soft tissues. Regarding the expander insertion techniques, no difference was observed between the tunnel and the flap approach. With the tunnel technique, fixation of the expander was more challenging compared to the flap approach due to restricted view and limited freedom of handling the expander. Based on the manufacturer's guidelines for intra-oral use of the expanders, insertion is recommended with the "tunnel" technique. This approach prevents a complete flap reflection for expander placement.

In an *in vivo* experiment, Abrahamsson et al. (2009) placed sub-periosteal osmotic soft tissue expanders in mandibles of rabbits. In each rabbit, two sites were assigned: test site in contact with the base of the expander, and control site which was the flat end of the expander, fixed by a mini screw and has no expanding capacity. Two weeks post-expansion, clinical inspection showed no signs of soft tissue dehiscence or infections and histological examination revealed periosteal expansion without any signs of inflammatory reactions or bone resorption. In fact, new bone formation at the edges of the expanded periosteum was evident, while there were no signs of bone formation in the control area.

In a following experiment, the authors applied the same animal model and protocol in order to evaluate the outcomes of post-expansion bone augmentation by GBR (with particulate onlay bone graft and covered either by titanium mesh or bioresorbable mesh) (Abrahamsson et al. 2010). Three months post-augmentation, it was evident that tissue expanders were able to create a sub-periosteal space and new bone formation was allowed underneath the mesh and at the edges of the expanded periosteum. The effect of soft tissue expansion on the outcomes of GBR with two different grafting materials was evaluated in an another animal study (Abrahamsson et al. 2011). In agreement with previous findings, soft tissue expanders were able to create a surplus of soft tissues including periosteum, which facilitated mucosal coverage of the bone graft without occurrence of soft tissue dehiscences. New bone formation was found under the titanium mesh regardless of the type of bone graft. Nonetheless, it must be noted that a lack of soft tissue dehiscences or related complications in this report may be attributed to the adopted extra-oral surgical approach. The authors chose such an approach as the access via the oral cavity in rabbits was restricted (Abrahamsson et al. 2010).

There are just few clinical data available which describe the mucosal expansion prior to bone augmentation; two case series (Kaner & Friedmann 2011; Mertens et al. 2015) and one randomised controlled clinical trial (Abrahamsson et al. 2012) could be found in literature.

In a randomised controlled clinical trial, Abrahamsson et al. (2012) applied sub-periosteal soft tissue expanders in ten patients requiring bone augmentation prior to implant placement. Two weeks post-insertion, the expanders have been removed and GBR was carried out with either a particulate onlay graft protected by titanium mesh and a collagen membrane (test group), or a cortical bone block graft, harvested from the ramus, without any previous soft tissue expansion (control group). The authors chose GBR as the bone-grafting method in the test group for two reasons: (i) predictable results have been reported with regard to bone fill (Degidi et al. 2003), and (ii) promising results after mucosal expansion have been described in previous animal experiments (Abrahamsson et al. 2010, 2011).

In the test group, two patients showed minor perforations of the soft tissues due to expander placement close to incision line. In these two cases, however, soft tissue expansion was sufficient to completely cover the bone graft with the mucosal flap, without any complications. In the control group, periosteal incisions were required to allow flap advancement and achieve full coverage of the bone grafts.

Changes in soft tissue profile of the attached gingiva were evaluated at baseline and 6 months after augmentation in both groups and additionally at post-expansion in the experimental group, by using an objective 3D metering device. This device is based on digital light stripe projection which deflects whenever the surface alters in topography.

During the procedure, a clinical picture is also taken. Deflection data are registered through a sensor and stored in a computer with appropriate software. Data are evaluated and displayed as a colour-coded picture of the topography (Wälivaara et al. 2007).

The software matched calibrated pictures for each patient in both groups at different time points. A line was drawn on the matched pictures of at the level of the attached gingiva and over the bone-augmented area. The lines opened up in a diagram which resulted in two or three curves depending on the number of the measuring occasions. These curves demonstrated soft tissue profile at the specific area where the lines were drawn. Alterations in soft tissue profile overtime were determined by measuring the height difference between the curves. The mean soft tissue profile gain at the attached gingiva level was 2.9 ± 1.1 mm when compared to baseline, while it decreased to 2.3 ± 2.1 mm at the time of implant placement, when compared with the starting point. The control group showed a soft profile change of 1.5 ± 1.4 mm at the time of fixture installation. Even if the test group showed increased gingival dimensions after surgeries, the differences have not been not statistically significant. The authors did not measure the total volume change in soft tissues, as they only wanted to determine overall stability of created soft tissues by evaluating soft tissue profile changes overtime. Although soft tissue profile became less prominent after healing of bone graft when compared to pre-augmentation soft tissue profile, this result was statistically insignificant.

Six months post-operatively, the test group showed a minimal resorption of bone graft in the vertical dimension of just 27% and a tendency for resorption in the horizontal aspect (14%). Corresponding to earlier findings in the literature (Chiapasco et al. 2006; McAllister & Haghighat 2007), vertical bone resorption was more pronounced than lateral one.

On the other hand, the control group showed a statistically significant bone resorption in both the vertical (42%) and horizontal (23.5%) dimension. Overall, bone resorption in the experimental group was less pronounced than that in the control group. However, the difference just reached statistical significance when smokers have been excluded from the calculation. Smokers have been included in the study as they might be candidates for such an approach in everyday clinical practice.

The favourable outcome with expansion could be attributed to the direct contact of the bone graft with periosteal progenitor cells. One might speculate that a reduced bone graft resorption in the test group is based on different augmentation modalities in test and control group.

Despite the satisfactory results reported with soft tissue expansion in animal and human clinical trials, the authors recommended further refinements of the soft tissue expansion technique particularly in smoking patients. Such refinements may mainly focus on the risk reduction in complications such as soft tissue perforation (Nyström et al. 2009; Lindfors et al. 2010).

Similarly, positive outcomes of pre-augmentation soft tissue expansion were reported by Kaner & Friedmann (2011) in a case series. In contrast to the previous study, the osmotic expanders have been placed in submucosal pouches. The rationale for the altered location was to prevent replacement of periosteum with collagen-rich connective tissues lacking osteoblasts and precursor cells, which can have negative effects on the healing of subsequent bone graft. We will elaborate more about this later in this review.

Of twelve patients enrolled in the study, two experienced soft tissue perforations by the expanders and had to be retrieved prior to final expansion. Perforation occurred due to infection 4 weeks post-insertion in one patient, while the choice of an oversized expander was the cause in the other one; a fact that emphasises the selection of an appropriate size of the expander. Perforated sites were allowed to heal for 6 weeks and then retreated with smaller expanders.

After 60 days *in situ*, all the expanders reached their final volume and vertical bone augmentation was carried out either with onlay grafting (autogenous bone block harvested from the ileum in three patients) or GBR (ramus graft covered with Bio-Oss and a collagen membrane, in nine patients). During removal of the expander, a surrounding capsule of soft tissue could be observed which did not show signs of inflammatory infiltration upon histological analysis. The expanded tissues showed good quality, and the space created by the expanders allowed a tension-free primary closure. Despite the occurrence of a minor exposure of bone graft in one patient following vertical augmentation in the posterior maxilla, spontaneous healing occurred following local debridement without any further complications. In the present study, pre-augmentation soft tissue expansion decreased the incidence of post-operative graft exposure to 4% in comparison with previous studies of vertical bone augmentation without prior soft tissue expansion of 23% (Verhoeven et al. 1997), 27.3% (Chiapasco et al. 2004), 25% (Proussaefs & Lozada 2005), 22% and 25% (Merli et al. 2007), and 33.3% and 50% (Roccuzzo et al. 2007). After 4–6 months of bone graft healing and just before implant placement, cone beam computed tomography (CBCT) analysis was performed and revealed a high vertical bone gain of 7.5 ± 2.4 mm, in comparison with findings from a recent systematic review, in which mean vertical bone gain was reported to be 4.8 mm with various augmentation methods (Jensen & Terheyden 2009). It must be noted that the amount of bone resorption was not measured in this case series. Bone biopsies were histologically analysed with micro-computed tomography (micro-CT), revealing appropriate bone volume density (BV/TV) with distinct trabecular structure. Implants have been placed after bone augmentation, with uneventful healing.

In an alternative case series, sub-periosteal osmotic expanders were applied by tunnel approach in eight patients with severe atrophy in the maxilla or mandible before bone augmentation (Mertens et al. 2015). Quality and quantity of newly created soft tissues were evaluated together with post-operative soft tissue-related complications such as perforation, infection, dehiscence, necrosis and pain. Expansion time varied between 20, 40 and 90 days depending on the size of the defect and dimensions of the expander. Upon insertion, patients reported a slight pressure in the area, but without any symptoms of pain. The only soft tissue-related complication was mucosal perforation accompanied with eventual pre-mature loss of the expander. Such complication occurred in two patients; one had a history of a previous trauma in the area of implantation, and the other had experienced a cleft surgery and did not follow the post-surgical instructions of abstaining of wearing the prosthesis. Both patients showed signs of mucosal scars prior to insertion of the expander. This suggests that case selection for soft tissue expansion is essential to avoid complications and that presence of scars at the surgical site might be a contraindication for soft tissue expansion. This hypothesis could not be confirmed in previous animal studies (van Damme et al. 1994, 1997), and soft tissue expansion was independent of the presence of scarred tissue. On the contrary, skin expansion decreased the limiting effect of

scar tissues on restriction of mid-facial growth (Edington et al. 1998), implying the option of expanding compromised soft tissues. Although the presence of scars might not be an "absolute" contraindication for expansion, it must be taken into consideration that compromised soft tissues usually have a lower expanding capacity compared to normal ones (Fang et al. 2013).

In contrast to the previously mentioned case series (Kaner & Friedmann 2011), retreatment with soft tissue expanders was not carried out. All other patients experienced uneventful healing free from any complications. Final expansion of the vestibular mucosa was achieved, and all the expanders reached their final size, limiting the amount of gain of keratinized mucosa. It has to be mentioned that the quality of the expanded tissues was lining and not masticatory mucosa. The authors explained that this might be related to the applied expansion technique, as all the expanders were placed in the vestibule and thus were only surrounded by alveolar mucosa.

After removal of the expanders, two recipient sites showed sign of resorption of the underlying bone. This observation did not have any adverse consequences, and the corresponding areas have been successfully augmented later on.

Vertical and/or horizontal bone augmentations were performed with either autogenous or synthetic block grafts. No periosteal releasing incisions were needed to achieve primary soft tissue closure over the bone graft, except in the two patients who experienced soft tissue perforation and pre-mature removal of the expanders. Post-operative healing of the grafts was uneventful. At the time of implant placement, all bone grafts were successfully healed and soft tissue quantity was sufficient to passively close the mucosal flaps. With the current expansion techniques, careful evaluation of the amount of keratinised and non-keratinised soft tissues is required in order to accordingly plan soft tissue expansion prior to bone or implant surgery. It has been reported that a lack of attached gingiva and presence of mobile soft tissues might impair the fixation of the expander (Park et al. 2013). On final clinical follow-up, no complications were reported and none of the placed implants were lost.

To summarise: Based on these three clinical studies, it can be concluded that soft tissue expansion prior to bone augmentation may reduce the risk of mucosal dehiscence with subsequent bone graft exposure. Additional randomised controlled clinical trials, with an adequate sample size and long-term follow-up, are needed to confirm these findings. Summary of these clinical studies are found in Table 2.

In two published case reports by Park et al. (2013), sub-periosteal hydrogel osmotic expanders were used prior to vertical bone augmentation in severely resorbed mandibular ridges. They were left *in situ* for either 3 or 6 weeks. At the time of bone grafting, tension-free and complete closure of the augmented bone with overlying soft tissues was achieved. After healing, the grafted bone was hard and intact clinically, and implants could be placed without any complications. Similar positive outcomes were documented with pre-augmentation soft tissue expansion, in a patient with significant bone resorption in the posterior area of the mandible (von See et al. 2010a).

Another indication where soft tissue expanders have been applied is the repair of lip and/or palate clefts. *In vivo* studies demonstrated variable outcomes with the applications of soft tissue expanders. In a rabbit cleft lip model, an overamount of soft tissue was generated by expansion of the labial surface area, resulting in reduced post-operative lip pressure and improved mid-facial growth (Edington et al. 1998). Conversely, in a cleft lip and palate model in cats (van Damme et al. 1997) even if soft tissue expansion of the palatal muco-periosteum was feasible, retardation of transversal growth was reported as an iatrogenic side effect from active expansion. Moreover, in a previous cat model by the same researchers, active expansion resulted in palatal bone resorption (van Damme et al. 1994).

In a clinical study, Kobus (2007) used hydrogel soft tissue expanders as an adjunctive in two-stage repair of cleft palate in children over the period of 15 months. The clinician intended to limit their palatal scarring and therefore preserve maxillary growth. Of the nineteen children enrolled in the study, seven ended up with fistulae despite the adjunctive application of soft tissue expanders. The high rate of fistulae was explained by the lack of silicon coating around the surface of osmotic expanders (first generation) which resulted in a super-quick expansion with concomitant wound dehiscences. Swan et al. (2008) criticised the fast expansion technique in children and stated that the available soft tissue expanders tend to expand equally in all directions (i.e. isotropic), which is not feasible in a confined area like the palate. They recommended that directionally dependent expansion must be developed to allow for swelling in transverse direction only.

A novel anisotropic self-inflating hydrogel tissue expander was recommended that can improve future clinical applications of soft tissue expansion in cleft palate defects, eyelid and nasal tip reconstruction.

This novel expander, based on methyl methacrylate and vinyl pyrrolidone designed to display anisotropy, showed a capacity for considerable expansion and a controlled modifiable expansion rate (Swan et al. 2011). Anisotropy was induced through compression of hydrogel copolymer at elevated temperatures (annealing), and expansion rate was controlled by incorporation of a semi-permeable silicone membrane, *in vitro*. Efficacy of this novel expander was later tested *in vivo*, by sub-periosteal implantation in hard palates of pigs (Swan et al. 2012). Uncoated and silicone-coated expanders were compared 6 weeks post-expansion. Similar to all published findings in the literature, uncoated devices resulted in rapid expansion causing muco-periosteal ulceration, while coated ones displayed a more controlled expansion. Coated expanders showed a significant increase in soft tissue volume without any evidence of acute inflammation. Formation of soft tissue capsule was present around these expanders, and expander-mediated erosion of palatal bone could be observed. Despite the promising results, clinical research is needed to investigate the outcomes of anisotropic expansion in specific intra-oral applications.

Technical guidelines for insertion of soft tissue expanders in pre-augmentation applications

The placement of soft tissue expanders in the oral mucosa is technique sensitive, and caution must be taken especially in tunnel techniques. Their use in a moist environment might influence the operation time, as soft tissue expanders start to swell once in contact with the fluids. Thus, placement of soft tissue expanders requires high technical skills of the surgeon. Screw fixation is mandatory to avoid migration when subjected to chewing or expanding forces. To facilitate screw fixation, osmotic expanders are fabricated with a flat end on one side, as shown in Fig. 5. This flat area has no expanding capacity. However, care must be taken that even if screw-fixed, the expander can still migrate if placed close to the incision line or mucosal perforation may occur as negative side effects (Manders et al. 1984; Radovan 1984; Wieslander 1991; Abrahamsson et al. 2012). Usually, expanders are

Table 2. **Summary of clinical studies on pre-augmentation soft tissue expansion**

Author & year	Type of study & no. of subjects	Treatment groups	Type of expander	Shape of expander & final volume or dimensions	Location of expander	Time needed for full expansion	Soft tissue complications during expansion	Soft tissue quality post-expansion
Kaner & Friedmann (2011)	Case Series (12)	Soft tissue expansion followed by bone augmentation in all patients	Second-generation hydrogel osmotic expanders	Hemisphere with 0.35 ml final volume or Round-ended cylinders with 0.24, 0.7, 1.3 or 2.1 ml final volume	Submucosal (in maxilla or mandible)	60 days	Soft tissue perforation in two patients, due to infection or oversized expander	Excellent quality with enough created space
Abrahamsson et al. (2012)	RCT (20)	Test Group (10): expansion followed by bone augmentation Control Group (10): bone Augmentation only	Second-generation hydrogel osmotic expanders	Shape: N/A Final Dimensions: 5.6 × 11 × 6 mm	Sub-periosteal (in maxilla or mandible)	14 days	Soft tissue perforation and projection of expander through incision line in two patients	Surplus amount of soft tissue
Mertens et al. (2015)	Case Series (8)	Soft tissue expansion followed by bone augmentation in all patients	Second-generation hydrogel osmotic expanders	Hemisphere or cylinder with 0.24, 0.35, 0.7, 1.3 and 2.1 ml final volume	Sub-periosteal (in maxilla or mandible)	20 or 40 or 90 days (depending on the size of the defect)	Soft tissue perforation in two patients with previous history of trauma or cleft surgery	Excellent soft tissue quality and quantity but no increase in keratinized gingiva

RCT, randomised clinical trial; NA, not announced.

removed after successful mucosal expansion and immediately prior to bone augmentation.

Tissue expansion can be done repeatedly in the same area (Kaner & Friedmann 2011), and increasing forms of expanders can be indicated in large defects (Mertens et al. 2015). These findings are confirmed by studies dealing with soft tissue expansion in plastic surgery (Roposch et al. 1999; Huo et al. 2009; Liu et al. 2011).

Effect of expansile pressure and location of the expander on the underlying bone

During the soft tissue expansion process, the underlying bone surface serves as a counterbearing area for the expansile stress exerted by expanders (Stuehmer et al. 2009). These pressures could evoke bone reactive changes, such as bone resorption.

There are conflicting findings in the literature about the reciprocal effects between soft tissue expanders and bone; while some studies reported about bone resorption (Hemmer et al. 1987; Antonyshyn et al. 1988a; Fudem & Orgel 1988; Tominaga et al. 1993; van Damme et al. 1994; El-Saadi & Nasr 2008; Mertens et al. 2015) or decreased bone density (Stuehmer et al. 2009), others did not observe any signs of bone loss (Uijlenbroek et al., 2011) or even documented new bone formation (Abrahamsson et al. 2009, 2010, 2011).

Despite these contradictions, bone resorption and deformation have been well documented with conventional expanders, used in children and adults (Hemmer et al. 1987;

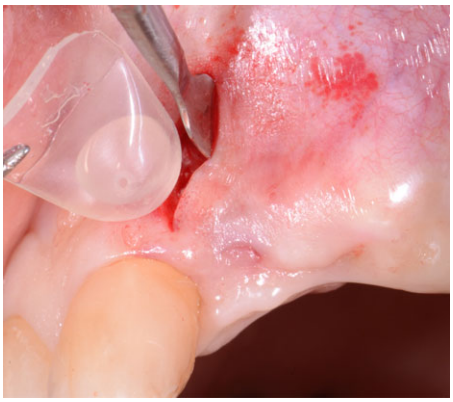

Fig. 5. Osmotic expander with a flat-end to facilitate screw fixation and prevent migration of the expander. Flat ends have no expansion capability. "*Courtesy of:* Rasperini, G. University of Milan, Department of Biomedical, Surgical and Dental Sciences, Foundation IRCCS Ca' Granda Polyclinic, Milan, Italy".

Signs of bone resorption post-expansion	Bone-grafting technique	Need for periosteal releasing incisions/flap advancement	Adverse outcomes post-augmentation	Analysis & investigation	Further findings	Other comments
No signs of bone resorption	Vertical bone augmentation with either autogenous block graft or GBR	Tension-free closure was achieved in all patients	Very low incidence of graft exposure (4%).	(i) Clinical (ii) Radiological (CBCT) (iii) Histological (iv) Micro-CT analysis of bone core biopsy	(i) Mean vertical bone gain highly increased (7.5 ± 2.4 mm) (ii) Encapsulation of all expanders on retrieval without any signs of inflammatory infiltrate on histological analysis (iii) Good bone volume density on micro-CT (0.1614 ± 0.0582)	(i) The authors did not measure amount of bone resorption post-augmentation. (ii) Patients who had perforations were retreated again with expanders after time for healing was allowed.
NA	Test Group: Horizontal and vertical bone augmentation with GBR Control Group: Horizontal and Vertical augmentation with autogenous block graft	Only in the control group	Test Group: statistically significant bone loss in vertical dimension only (27%) ($P = 0.04$) Control Group: statistically significant bone loss vertically (42%) and horizontally (23.5%) ($P = 0.01$, $P = 0.024$, respectively)	(i) Clinical (ii) Objective 3D metering device	(i) Test group showed less vertical and horizontal resorption of the bone graft in comparison with the control group, and this was statistically significant with the exclusion of smokers. (vertical, $P = 0.12$, horizontal, $P = 0.049$). (ii) Soft tissue profile was less prominent after healing of bone grafts, but this was statistically insignificant.	(i) Authors excluded smokers from the final analysis. (ii) Authors attributed better results in control group either to soft tissue expansion or to different grafting techniques between groups. (iii) Authors did not measure the final gained soft tissue volume.
Two recipient sites showed signs of bone resorption, due to pressure from expansion, without further consequences	Vertical and/or horizontal augmentation with either autogenous or synthetic block grafts	Only in the two patients who pre-maturely lost the expanders	None. All grafts were successful at the time of dental implant placement	Clinical	(i) Encapsulation of all expanders on retrieval (ii) Expansion time depended on the defect size and expander dimensions	(i) Patients reported slight pressure when the expanders were placed, without pain. (ii) Patients who had perforation were not retreated with expanders. They were only treated with bone augmentation. (iii) Expanders improved quantity and quality of soft tissues but did not alter the type of the original soft tissue subjected to expansion

Fudem & Orgel 1988; Paletta et al. 1989; Penoff 1990; Schmelzeisen et al. 1999). Expansion-mediated bone deformity might be a minor clinical finding (Sinow et al. 1991). Nevertheless, in some cases the bone deformations are not completely resolved after expander removal and deformities will remain (von See et al. 2010b). The causative underlying effect might be the pressure peaks associated with conventional expanders. It is well documented that osteoclastic activity increases in areas subjected to higher pressure (Tominaga et al. 1993), especially when a certain threshold level has been exceeded (Sato et al. 1998).

Early studies suggested that decreased bone thickness and erosion are usually evident on the bone surface below the expander (Johnson et al. 1993), while increased bone thickness, volume and bone deposition are apparent at the periphery of the expanders most of the time, as a part of hyper-compensation mechanism (Johnson et al. 1993). Hyper-compensation occurs in the form of increased bone apposition and micro-circulation (Svindland et al. 1995), following hypo-perfusion of the underlying bone when the periosteum is elevated (Kowalski et al. 1996) for expander placement.

To decrease the risks for bone resorption, applied forces must be distributed over a large surface area, like it happens with second-generation expanders. Nonetheless, bone resorption can occur with osmotic expander when placed sub-periosteally, even without pressure peaks. Sub-periosteal placement of hydrogel expanders may impair micro-circulation of the bone (Rucker et al. 2005), which in turn causes bone resorption (Hemmer et al. 1987) due to limited nutrition via the periosteum (Chanavaz 1995).

Bone resorption with sub-periosteal expanders was confirmed in a rat model (Stuehmer et al. 2009); a significant decrease in bone density and thickness in the area underneath the expander was observed 21 days post-expansion. This was attributed to the position of the expander directly on bone.

Similarly, Mertens et al. (2015) observed bone resorption with sub-periosteal expanders in two patients but without any negative effects on the final outcomes. Interestingly, although the authors attributed these findings to pressure on bone, one of the patients had been fitted with two expanders but showed bone resorption under one expander only. The authors did not interpret this finding.

In contrast, Abrahamsson and co-workers suggested that placing the expanders in a sub-periosteal location induced slow expansion of the periosteum which resulted in new bone formation at the periphery of the expanders (Abrahamsson et al. 2009, 2010, 2011) without any signs of bone resorption underneath these devices. They assumed that the slow expansion of the periosteum activated osteogenic cells which enhanced bone formation. In fact, different studies confirmed that lifting the periosteum slowly can result in new bone formation, as it has been described for periosteal distraction (Schmidt et al. 2002; Kessler et al. 2007; Sencimen et al. 2007). In an attempt to prevent direct contact between expanders and bone, Kaner & Friedmann (2011) implanted the expanders in submucosal pouches, which resulted in positive outcomes, without any signs of bone resorption.

Further findings from the literature suggest that bone resorption is in fact related to the "amount" of pressure forces exerted on the bone surface when the expanders are placed sub-periosteally in direct contact with bone and not on their position per se. Permanent pressure on bone surpassing a certain threshold can result in bone necrosis (Carlsson 2004). The maximum force exerted by expanders is reported to be 32.4 kPa (Wiese 1993), and it has been demonstrated that persistent compressive pressure of a threshold surpassing 6.86 kPa leads to significant bone resorption due to reduced perfusion (Sato et al. 1998) in rats. However, critical pressure force is expected to be much higher in humans (Mertens et al. 2015). This might explain why resorption with sub-periosteal osmotic expanders was reported in rats (Stuehmer et al. 2009), but not in humans (Abrahamsson et al. 2012). In a rabbit model, there were no signs of bone resorption due to exerted pressure on bone (Abrahamsson et al. 2009), which proposes that critical pressure also differs between different animals.

Distribution of pressure over a large area could minimise the probability of surpassing a certain threshold and thus reduce the risks for bone resorption. von See et al. (2010b) used a calvarial rat model to investigate whether simultaneous insertion of mechanical devices along with the expanders could result in a better distribution of the load on bone and over a larger surface area. Four groups were compared: expanders alone, expander with underneath titanium plate, expander with underneath titanium mesh and control group. Twenty-one days post-expansion, micro-CT images and histological analysis revealed significant decrease in hydroxyapatite density and marked lacunae beneath the osmotic hydrogel expanders when they were applied without underlying titanium mesh or plate, while such decrease in bone density was reduced when titanium mesh was placed, and totally prevented with titanium plate. Moreover, bone thickness was decreased with expanders solely or expanders implanted on titanium mesh, but not with expanders placed on titanium plates. A compensatory increase in bone thickness at the peripheries could be observed in all the test groups, but not in the control group. Although titanium mesh and titanium plate acted as pressure distributors, titanium plate disseminated forces more effectively because expanders directly placed on bone or titanium mesh induced connective tissue lacunae in the bone underneath the expander. As a consequence, morphologic changes can only be prevented with the utilisation of titanium plates, as bone resorption cannot be avoided with titanium mesh underneath the expander.

In conclusion, bone resorption has been very well documented with conventional expanders, but inconsistent with osmotic expanders. With sub-periosteal expanders, bone resorption has been reported *in vivo* in rats, due to low pressure threshold in small animals, while there were conflicting findings in studies on humans. Further clinical investigations are mandatory to determine the pressure threshold of expanders in humans, which, if surpassed, might cause bone resorption. Evaluation of the bone surface reaction to applied soft tissue expansion is also needed to confirm the preliminary findings from the present clinical studies.

Effect of connective tissue capsule surrounding the expanders on bone augmentation

Connective tissue capsule formation is a common finding around the expanders when they have been retrieved (Pasyk et al. 1984). Data from the early literature suggest that dense fibrous capsule can develop around the tissue expanders and completely surround them within few days after insertion (Austad et al. 1982; Pasyk et al. 1982, 1988; Argenta et al. 1985). On the other hand, the capsule thickness rapidly thins out after expander removal (Johnson et al. 1993). These findings could not be confirmed by recent studies which showed that soft tissue capsule does not form unless the expander is left in location for more than 2 weeks (Kaner & Friedmann 2011; Abrahamsson et al. 2012; Mertens et al. 2015).

In the previously mentioned study, Kaner & Friedmann (2011) placed soft tissue expanders in a submucosal pouch without elevation of the periosteum, to avoid replacement of periosteum with fibrous connective tissue. Soft tissue capsule may negatively affect the healing of bone following augmentation. Periosteum is a fundamental source for osteoblasts and their precursor cells (Allen et al. 2004).

Encapsulation of sub-periosteal expanders can be avoided if they are left *in situ* for just a short period of time; Abrahamsson et al. (2012) removed sub-periosteal expanders 14 days post-insertion without any signs of fibrous tissue encapsulation. This had positive effects on bone augmentation, documented in their rabbit models; there was an evident direct contact between progenitor cells populating the periosteum and the bone graft in histological analysis (Abrahamsson et al. 2010, 2011). Although encapsulation was not reported, it was evident in earlier rabbit models, in which all expanders were covered by collagen-rich capsule within 2 weeks after insertion (Abrahamsson et al. 2009).

Encapsulation was evident when sub-periosteal expanders were retrieved after 20, 40 or 90 days (Mertens et al. 2015). Fibrous tissue encapsulation seems to be inevitable if the expanders are left in place for a long time, regardless of their location; it was obvious with submucosal soft tissue expanders that were left in location for 60 days (Kaner & Friedmann 2011).

Based on these findings, it was suggested that caution must be taken not to leave sub-periosteal expanders for a long time; otherwise, fibrous connective tissue replacement of the periosteum should be expected (Abrahamsson et al. 2012).

Mertens et al. (2015) did not report any negative outcomes following bone augmentation and implant placement, despite the development of a soft tissue capsule around the sub-periosteal expanders. A recent *in vivo* study revealed that, although sub-periosteal implantation of expanders resulted in complete ischaemia of the periosteum and was replaced by fibrous connective tissue within 14 days, these tissues had significantly higher density of micro-vessels than a healthy periosteum which did not have any negative effects on vascularisation to the bone (von See et al. 2010c). Such findings might justify bone augmentation immedi-

ately following the completion of soft tissue expansion, even if there is complete replacement of the periosteum with a fibrous tissue capsule. Earlier studies included recommendations for a delayed bone-grafting procedure after soft tissue expansion (LaTrenta et al. 1988).

More clinical trials are needed to evaluate the effect of connective tissue capsule formation on subsequent bone augmentation.

Effect of soft tissue expanders on micro-circulation and soft tissue vascularisation

Integrity of vascularisation is important to ensure successful outcomes of the surgical procedures. Different studies have been conducted to evaluate the effect of soft tissue expansion on vascularisation of the soft tissues.

In an *in vivo* study on beagle dogs, Kaner et al. (2014) evaluated the effect of submucosal soft tissue expansion on mucosal microcirculation. Following surgical interventions, there is a hyperaemic response of the periosteal and *supra*-periosteal blood vessels during the first 3 days post-operatively (Caffesse et al. 1981; Nobuto et al. 2005). Although micro-circulation was reduced after local anaesthesia, there was a reduction in post-operative hyperaemic response during the first 3 days post-surgery. This fact may be attributed to minimal surgical trauma as preparation of a submucosal pouch only requires a minimally invasive surgical approach without any need for elevation of the periosteum. The study conductors concluded that microcirculation is minimally and momentarily disturbed by insertion of expanders, which explains the positive outcomes with submucosal expanders, in previous investigations (Kaner & Friedmann 2011).

In another animal model on beagle dogs, the authors evaluated micro-circulation in vertical bone augmentation following soft tissue expansion (Kaner et al. 2015). Augmentation surgery impaired micro-circulation in control group, but did not cause further decrease in sites treated with expanders, beyond that of local anaesthesia. Two weeks post-augmentation, micro-circulation was significantly lower for the control group, compared to test group, and although no signs of wound dehiscence were reported in the test group (with expanders), eight wound dehiscences were evident in the control group (without expanders). Based on that study, it seemed that soft tissue expansion may lower the impairment of micro-circulation caused by vertical ridge augmentation and reduce the incidence of soft tissue dehiscences.

Even if expander losses were low in a case series of patients, 30% of the expanders were lost in this animal study. The authors attributed this finding to possible continuous uncontrolled mastication on the surgical sites, despite the proper surgical execution.

In another *in vivo* study on rats, von See et al. (2010d) reported a higher density of micro-vessels in the soft tissue surrounding the augmentation material when pre-augmentation soft tissue expansion was utilised, in comparison with grafted area without a prior soft tissue expansion. This was in agreement with early studies which confirmed an increase in the vascularity of the expanded tissues. Histological findings revealed that rapid angiogenesis is evident with increased number of blood vessels at the junction between connective tissue capsule and host tissues, which contributes to an actual increase in the vascularity of the expanded soft tissues (Johnson et al. 1993). Subsequent bone augmentation did not have any influence on functional micro-vessel density caused by soft tissue expansion. Complete osseo-integration of the bone graft was possible when the mucosal perfusion around the augmentation area was not compromised (von See et al. 2010d). High vessel density of soft tissues seems to play a role in blood supply to the underlying bone (Chanavaz 1995).

Absence of periosteal perfusion was observed in bone augmentation without previous soft tissue expansion caused by surgical dissection of the periosteum (Kowalski et al. 1996). Additionally, the periosteum will be subjected to tensile forces during the surgical procedure which further impairs the patency of the vessels (von See et al. 2010d).

It can be concluded that, regardless of the location of the expanders, tissue expansion tends to increase vascularisation of the soft tissues and also reduces adverse effects on micro-circulation following bone augmentation.

Summary of relevant *in vivo* studies are presented in Table 3.

Long-term outcomes of applications of osmotic hydrogel soft tissue expanders

As the application of soft tissue expanders for intraoral mucosal expansion is relatively new, no long-term results are available. Clinical guidelines may be extrapolated from studies that describe the use of osmotic expanders in plastic surgery.

Chummun et al. (2010) published their 5-year experience with soft tissue expanders through retrospective data collection. Ten patients have been treated with soft tissue expanders for either alopecia, scars or burn contracture. Six patients had an uneventful post-operative healing, and the required amount of soft tissues was obtained without any complications. The other four patients developed different degrees of wound infection. Based on the high complication rate, the authors suggested that identifying a suitable anatomical location and proper case selection seems to be mandatory in order to avoid any complications. Similarly, Obdeijn et al. (2009) reported a high complication rate in a 3-year clinical experience. From nine patients treated, complications of infections, ischaemia of the skin and expander migration were reported in five patients. In two cases, complications were attributed to previous irradiation in the area where the expander was inserted. As a matter of fact, previous irradiation and infected areas are contraindications for implantation of tissue expanders (Ronert et al. 2004). However, if using soft tissue expanders are indicated, radiation therapy should only start after the completion of the expansion phase (Ronert et al. 2004).

Obdeijn et al. (2009) expanded scalp skin in five patients, and confirmed by previous data, they found high complication rate when expanders are applied in the head and neck areas (Antonyshyn et al. 1988b). Nonetheless, data from a 15-year retrospective study revealed that a high complication rate with head and neck soft tissue expansion could be noticed, but the severity of complications was of minor importance (Belghith et al. 2012).

The authors recommended that indications for soft tissue expansion must be considered carefully, not to change the advantages of tissue expansion into a disadvantage by increasing complications (Obdeijn et al. 2009).

A more positive experience with soft tissue expanders was published by Ronert et al. (2004) in which they used expanders in 58 patients for different extra-oral indications, mainly in breast reconstructions, over the period of 4 years. They reported a success rate of 81.5% in expanders without a silicone envelope, while it was up to 91% with silicone-coated expanders. The authors considered the final outcome as successful when

Table 3. **Summary of *in vivo* studies on pre-augmentation soft tissue expansion**

Author & year	Animal model & no. of subjects	Treatment groups	Type of expander	Shape of expander & final volume or dimensions	Location of expander	Time needed for full expansion	Analysis & investigations	Important findings
Abrahamsson et al. (2009)	Rabbits (8)	In each rabbit, two sites were involved: Test site: soft tissue expander Control site: the flat end of the expander, which has no capability for expansion.	Second-generation hydrogel osmotic self-inflatable expanders	Shape: NA Final Dimensions: 5.6 × 11 × 6 mm	Sub-periosteal (mandible, extra-oral approach)	14 days	(i) Clinical (ii) Histological	(i) No signs of soft tissue dehiscence or infections (probably due to extra-oral approach). (ii) No inflammatory infiltration. (iii) Connective tissue encapsulation. (iv) New bone formation at the edge of expanders. (v) Surplus amount of soft tissue was created. (vi) No signs of bone resorption as due to pressure.
Stuehmer et al. (2009)	Rats (18)	First group: soft tissue expander in direct contact with bone Second group: soft tissue expander separated from bone by polydioxanone (PDS) foil Third group: control	Second-generation hydrogel osmotic self-inflatable expanders	Hemisphere, 0.7 ml	Sub-periosteal (Calvaria)	21 days	(i) Histological (ii) Radiological (micro-CT) (iii) Immunohistochemistry	(i) No signs of inflammatory reactions. (ii) Significant decrease in hydroxyapatite density in first group. (iii) Statistically significant decrease in bone thickness beneath expanders in first and second groups ($P < 0.05$). (iv) Bone thickness at the peripheries did not change in all groups.
Abrahamsson et al. (2010)	Rabbits (13)	Soft tissue expander followed by GBR (onlay bone graft + either titanium mesh or bioresorbable mesh) in all rabbits	Second-generation hydrogel osmotic self-inflatable expanders	Shape: NA Expanders increased 6 times their original volume (initial dimensions were 2.5 × 7.5 × 3 mm).	Sub-periosteal (mandible, extra-oral approach)	14 days	(i) Clinical (ii) Histological	(i) Soft tissue dehiscence was recorded in two of the sites with bioresorbable meshes. (ii) Surplus amount of soft tissue was created. (iii) Mean bone fill was 65% under the titanium mesh and 85% under the bioresorbable mesh ($P < 0.05$). (iv) New bone formation was in direct contact with both types of mesh.
von See et al. (2010b)	Rats (28)	First group: soft tissue expander only Second group: soft tissue expander placed on titanium mesh Third group: soft tissue expander placed on titanium plate Fourth group: control group	Second-generation hydrogel osmotic self-inflatable expanders	Hemisphere, 0.7 ml	Sub-periosteal (Calvaria)	21 days	(i) Radiological (Micro-CT) (ii) Histological	(i) Hydroxyapatite density was significantly decreased beneath the expander when no pressure distributor was used, or with underneath titanium mesh. (ii) Compensatory increase in hydroxyapatite density at the periphery when no pressure distributor was used, or with titanium mesh only. (iii) No change in hydroxyapatite density with titanium plates. (iv) Marked destruction underneath all the expanders. (v) Increased bone thickness at the periphery underneath all expanders (compensatory). (vi) Bone beneath titanium plate was comparable to control histologically
von See et al. (2010d)	Rats (16)	Test group: soft tissue expansion followed by bone augmentation with autogenous bone graft Control group: bone augmentation with autogenous bone graft only	Second-generation hydrogel osmotic self-inflatable expanders	Hemisphere, 0.7 ml	Sub-periosteal (clavaria)	21 days	(i) Histological (ii) Intravital microscopy (microcirculation monitoring)	(i) In control group: bone graft did not become completely integrated with the underlying bone. (ii) In test group: complete osseointegration of bone graft, vascular connection between bone graft and underlying bone, numerous osteoblasts and active osteocytes. (iii) Functional micro-vessel density soft tissue overlying bone graft was significantly higher in test group ($P < 0.05$).

Table 3. *(continued)*

Author & year	Animal model & no. of subjects	Treatment groups	Type of expander	Shape of expander & final volume or dimensions	Location of expander	Time needed for full expansion	Analysis & investigations	Important findings
Abrahamsson et al. (2011)	Rabbits (11)	Soft tissue expansion followed by GBR (autogenous particulate bone or Bio-Oss covered by titanium mesh overlied by collagen membrane)	Second-generation hydrogel osmotic self-inflatable expanders	Shape: NA Final dimensions: 5.6 × 11 × 6 mm	Sub-periosteal (mandible, extra-oral approach)	14 days	(i) Clinical (ii) Histological (iii) Scanning electron microscopy (SEM)	(i) No signs of dehiscence infections, or perforation. (ii) No signs of inflammatory response. (iii) New bone formation under mesh. (iv) Mean bone fill was 58.1 ± 18% with autogenous bone and 56.9 ± with Bio-Oss. (v) Surplus amount of soft tissue was created. (vi) Generated bone was denser with Bio-Oss.
Kaner et al. (2014)	Dogs (10)	Soft tissue expansion only	Second-generation hydrogel osmotic self-inflatable expanders	Cylinder, 0.7 ml	Submucosal (mandible)	42 days	Laser Doppler flowmetry (LDF)	(i) Local anaesthesia caused significant decrease of blood flow at baseline ($P < 0.05$). (ii) No additional significant decrease of blood flow upon completion of surgery. (iii) Blood flow showed significant increase 1 and 3 days post-surgery when compared to measurement post-anaesthesia ($P < 0.05$). (iv) Submucosal implantation of soft tissue expanders resulted in momentary disturbance of micro-circulation.
Kaner et al. (2015)	Dogs (10)	Test Sites: soft tissue expansion followed by vertical augmentation with GBR (onlay autogenous graft + granular biphasic calcium phosphate + resorbable membrane) Control sites: bone augmentation as in test sites but without prior expansion	Second-generation hydrogel osmotic self-inflatable expanders	Cylinder, 0.7 ml	Submucosal (mandible)	35 days	(i) Laser Doppler flowmetry (LDF) (ii) Receiver operating characteristic (ROC) curves	(i) Primary closure was achieved in test groups while there was a need for releasing incisions in control group. (ii) Surplus amount of soft tissue was created in test group. (iii) In control group, 8 dehiscences were found. (iv) Post-augmentation, test sites showed significantly better perfusion than control sites without preceding soft tissue expansion ($P = 0.012$). (v) Three days post-surgery, perfusion was still significantly decreased in control sites ($P = 0.005$), while microcirculation in test sites had returned to pre-surgical levels. (vi) Micro-circulation levels post-augmentation significantly predicted subsequent would dehiscence ($P = 0.006$)

NA, not announced.

there was adequate soft tissue gain with good final aesthetic appearance.

Regarding soft tissue expansion in paediatric patients, high complication rates, most commonly infection, have been reported (Pisarski et al. 1998; De Agustin et al. 1993; Iconomou et al. 1993; Gibstein et al. 1997; Neale et al. 1998; Hurvitz et al. 2005). Complication rates in children undergoing soft tissue expansion have been reported to be high, ranging between 20% and 40% (Friedman et al. 1996).

According to published data, the source of infections could be distant from the location of the expander (Mason et al. 1999), such as endogenous sources like pharyngitis or otitis media, which suggest the relocation of the aetiological bacteria from the infection site to the expander through dissemination by haematogenous or lymphatic pathways. Despite using conventional soft tissue expanders which already increase the risk of infections, Adler et al. (2009) concluded that infection did not hamper further expansion or successful reconstruction, in concordance with other reports (Radovan 1984; Antonyshyn et al. 1988a).

Although the role of antibiotics to prevent bacterial seeding on the expander from remote infected sites still needs to be evaluated, it might be preferable to prescribe antibiotics in individuals with high risk of developing infections. This might be valid as well for the application of intra-oral soft tissue expanders. Additionally, we suggest that expander placement adjacent to teeth must be prepared by a careful periodontal screening and treatment in order to avoid wound infections.

To avoid expander infection, Wacke et al. (2011) studied hydrogel osmotic expanders as a drug delivery system for antibiotics, *in vitro*. Expanders were incubated with either tobramycin or ofloxacin, in a setting that simulates the orbit of a newborn. Results showed that antibiotic release from the expander to the surrounding environment was sufficient and in effective concentrations which can be useful in preventing post-implantation infections in future clinical applications, and also eliminating the adverse effects associated with the administration of systemic antibiotics. Such expanders should also be tested for intra-oral applications, as they might decrease infection complication rates.

For intra-oral applications, soft tissue expansion should be avoided in irradiated and actively infected sites.

Recommendation and future directions

Applications of soft tissue expanders prior to bone augmentation and placement of endosseous implants are still in a preliminary phase. Despite the initial promising results from the presented clinical studies, further clinical investigations are mandatory to work out clinical guidelines and protocols to define indications and contraindications for pre-augmentation applications. The effect of soft tissue expansion to the bone needs to be determined, as well as the effect of the location of the expander and the amount of applied pressure.

The relationship between soft tissue expansion and tissue biotype (thick vs. thin) has not been addressed yet in the literature. Thus, the effect of tissue biotype on the final outcomes of pre-augmentation soft tissue expansion needs to be investigated. Moreover, the relationship between the rate of expansion and tissue biotype and the determination of a suitable expander insertion technique for each biotype should be evaluated as well.

Conclusion

An ideal expander requires the following characteristics, as described by Mazzoli et al. (2004): (i) it should be easy to manipulate and place especially in sites with small access, (ii) it should expand gradually and controllably over a short period of time, yet tolerable on long term, without inducing pressure spikes resulting in complications, such as infections and extrusion of expanders. These requirements are met with the osmotic expanders, mainly second generation. Based on the results presented in this review, there is promising, albeit preliminary information regarding the benefits of pre-augmentation soft tissue expansion. The previous findings cannot be generalised due to relatively small sample size. Further clinical trials with a larger sample sizes and long-term follow-up are needed before implementing soft tissue expanders into everyday clinical practice.

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Conflict of interests

The authors declare no conflicts of interest.

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