Ph.D. Thesis

Substitution of Complex Tissue Losses in Maxillofacial Surgery

Dr. Redl Pál

University of Debrecen Medical and Health Science Centre

Institute of Dentistry

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Introduction

With a concerted activity of complex anatomic structures, dentition, soft tissues, skeletal and nervous system, the maxillofacial region ensures a functional and esthetic equilibrium which is decisive for the individual throughout their life.

The tissue integrity of the region may be damaged due to several etiological factors. The relative balance of simple cariologic or paraodontological states may be overthrown even by meteorological changes; activated inflammations and reactive oxygen intermediaries produced by periapical granuloma phagocytes may lead to tissue damage. These may be followed by tooth removal, abscess formation, soft tissue scars impairing oral health.

The substitution of permanent tooth loss represents a difficult chapter in prosthodontics. Besides, functional and dentition rehabilitation may become extremely difficult in cases of accidents and in fractures complicated by severe soft tissue damage. The loss of posterior teeth, subsequent alteration in the supporting system, the shift from bridge substitution to removable prosthesis have a strong psychological effect on the patient. Several surgical methods are in use for the support of prosthetic care of posterior tooth losses using a fixed system. Implantation, (both enossal and subperiostal) as well as sinus elevation aim to find a solution to these problems. In addition to these rather expensive interventions, another alternative would be the autotransplantation of the tooth or that of the tooth together with the surrounding osseous tissue. The integrity of the periodontal ligamentous apparatus is a crucial issue in tooth transplantation.. If it is injured, ankylotic fixation and resorption of the tooth will follow, which is considered to be a failure in the long run.

Dental implants have opened a new chapter in prosthetic design. After planning the substitution system in the oral cavity, we have to precise the site of the

pillars in the mandible. To do this, we need further information on the depth of the processus alveolaris, the state of the mucous membrane and the pneumatization of the sinus maxillaris. Traditional X-ray pictures, though provided useful information, did not give all the necessary data on the bones. That is why it was essential to introduce diagnostic methods widely used in other fields medicine into dental diagnosis, such as multidimensional computer tomography.

The number of neoplastic diseases has been steadily growing in the past decades. Hungary is the first in morbidity and mortality rate resulting from oral neoplasms in Europe. The situation is worsened by the fact that more than 50% of the patients are diagnosed and treated at a late stage (stage III-IV). The therapeutic results are much worse at these stages than in early or precancerous stages. Surgical treatment often results in amputation especially in advance stage diseases with sacrifying facial, oral and mandibular structures.

The closure of expanded surgical defects, the replacement of lost tissues have undergone revolutionary changes in the last three decades. Due to the developments in surgical techniques and intensive anesthesiology, the terms 'resectability' as a technical term and 'operability' as a term characterising the endurance of the individual, have received a wider sense.

The main task of a surgeon is tissue replacement as written records dating from 600 BC already testify it. We can read about nose replacement with temporal lobe in Sushruta Samhiat. Since then, besides island-like and lamellar epidermal grafting, several methods using lobes have come into practice. Experience has made it a rule that the length of the lobe cannot exceed its width or the lobe cannot be longer than the double of its width even in areas with the best blood supply. To increase lobe length, Filatov elaborated cylindric lobe grafting**,** then a method of retention was employed.

The use of deltopectoral skin lobes first described by Bakamijan broke the standard rule and revolutionarised plastic surgery. Due to abundant blood

supply, the lobe based on the a. thoracica interna intercostalis made prosthetic techniques much safer. It is a well known fact that the blood supply of the skin is ensured by the so-called musculocutan perforans originating from the muscle below it. This was recognised and elaborated for use in clinical medicine by a Columbian surgeon, Ortichochea. In the head and neck region the following musculocutaneous lobes can beconsidered: platysma, sternocleidomastoideus, temporalis, trapezius, pectoralis major, latissimus dorsi. Several Hungarian authors have described their use. The heroic surgical interventions performed due to head and neck neoplasms may be accompanied by various severe complications, among them the development of pharyngocutaneous fistulas, which are undesirable side effects of the surgery of expanded oral-pharyngeal and laryngeal neoplasms. Their incidence is 2-66% in the literature. The solution of cases not healing by conservative treatment is a difficult surgical task.:random lobes next to the fistula and axial lobes found in the region may be used for this purpose. For reconstructive surgery, musculocutaneous lobes and fasciocutaneous lobes transplanted by microsurgey may be employed.

In such cases, a significant alteration in speech, mastication, bite forming and swallowing is seen. The individual's appearance changes, surgical traces on the face are conspicuous. This may have more serious psychological consequences in young patients: deterioration in the quality of life and social isolation due to esthetic injuries.

Several problems may emerge during the rehabilitation of tissue deficiencies in the maxillofacial region. The structural changes resulting from edentation may usually be corrected by up-to-date prosthodontic methods in an acceptable way for the patient. Complex rehabilitation – including hard and soft tissue substitution, implantation for anchoring dental prostheses and permanent prosthetic rehabilitation - is essential after resection of tissue deficiencies resulting from trauma or oral neoplasms.

The surgical interventions in the maxillofacial region are always done in an infected region in practically each case. There are relatively few cases where the area under surgery would not communicate with the oral cavity, paranasal sinuses or salivary glands. In mandibular and maxillar fractures - due to the intensive pain – the self purification of the mouth changes immediately and the number of bacteria in the oral cavity rapidly increases. Malignant neoplasms usually contain nephrotic areas infected by pathogenic bacteria. Since contamination of the surgical area is unavoidable during the intervention, the treatment of inflammations and prevention of wound infections are extremely important in maxillofacial surgery. Further rehabilitation includes phoniatric, logopedic and physical therapy.

Aims:

1. To find relationships between the development of chronic inflammations and the severity of the resulting tissue damage and environmental effects.
2. To elaborate up-to-date methods for the surgical support of tooth loss restoration autoplastic surgery, dentoosseal autotransplantation based on well described indications). To examine the effect of the method on the survival of the paradontium.
3. To map the possibilities of computer tomography (CT) examinations for the detection of mandibular and maxillar bones during implantation planning. To compare traditional X-ray technics and CT in preimplantologic diagnosis.
4. Complex interventions require resection of the mandibula. My further aim is to evaluate tissue parameters before rehabilitation that influence the planning of these interventions, e. g., the measures of the bone helix **.**
5. To create an integrated range of activities which, in the case of resulting tissue loss and functional damage ensures the best possible level of rehabilitation for the patient. To achieve this, we wish to create the conditions for and initiate the practice of routine surgical interventions that

have been in use in the past twenty years. We analysed the most important parameters of the tissues used for substitution , such as measurability, width, flexibility, circulation. We put into practice oral neoplasm surgery and introduced the revolutionary technique of using musculocutaneous and osteomusculocutaneous pedicle lobes and routine employment of microsurgical methods in the restorative surgery of the anatomical regions.

6. To analyse the secretion of antibiotics in the saliva, since in the majority of cases, maxillofacial surgery is performed in severely or facultatively infected areas, to investigative the economic aspects of treatment.

Material and Method

1. **Measurement of reactive oxygene intermediaries and environmental effects on inflammatory processes**
2. 1.1. Measurement of reactive oxygene intermediaries:
   We analysed 22 surgically removed periapical granulomas. Tooth roots had been previously treated. The granulomas were cut into two halves, one half was used for the histological diagnosis of periapical granuloma, the other half for the analysis. The control material consisted of the gingival tissue taken at the extraction of molars of eight healthy patients with pulpitis. The tissue samples were homogenized in physiological salt solution.. Protein content was measured by Lowry et al method (1951), the end product of lipid peroxidatin, malonaldehid ((MDA) concentration by Placer et al method (1966). Superoxide dismutase (SOD) activity was measured by Misra and Fridovich method (1972), glutation peroxidase (GSH-PX) activity by the method described by Chiu et al (1976). The results are given in standard $\pm$ deviation. Significance levels were determined by Student t-test after normal distribution had been controlled by Geary test. Standard deviation values of the groups were compared by F-test.

1.2.Examination of environmental effects on the activation of inflammatory processes.

By studying the daily meteorological reports between 1 November 1985 and 31 October 1990 we examined the frontal passages (warm, cold, stationary, occlusial fronts, cyclone and anticyclone) for each day. Using the treatment register of the Unit of Oral Surgery we counted the number of patients admitted with dental abscess. The relationship between the incisions performed and the weather conditions was determined by linear correlation coefficients. The results are given in 10 day and 1 month periods.

2. Analysis of dentoosseal autotransplants in animal experiments:

2.1 Description of the intervention

The first right premolar tooth of 10 dogs was decrowned, the extirpation of the root pulp and the elaboration of the root canal were followed by root filling. After lobe regeneration, the tooth-bone entity was extracted as a whole. This was placed in a physiological salt solution until the antagonistic premolar was similarly removed then it was seated in the other's place and the wound was closed using the gingival lobe. The animals received antibiotic treatment for 7 days following the surgery.

2.2.Histological and histochemical examinations:

The transplants were examined 3 months following surgery. After the removal of the surgical areas of the mandibula and maxilla, the transplants were fixed in 10% buffered formalin. Decalcination was done at room temperature in 1N hydrochloric acid and 10% buffered solution of EDTA (pH:7,4). After imbedding and incision, haematoxylin-chromotrop dying was employed and the next premolar was used as a control. Collagen examination was done by using the topo-optical method. Collagenous fibers were indicated by Weigert-haematoxylin, picrosirius Red 3B dying, which is an additive topo-optical reaction. The evaluation of topo-optical reactions was

done by Reichert-Zeopton microscope in monochromatic light. The results were compared by t-test.

3. Computer tomography:

In the preparatory phase preceding implantation, computer tomography (CT) was performed to measure mandibular conditions using a Siemens DR3 CT. With the help of the CT software, from the axial slices selected from the lateral topogram, secondary images were prepared in all the planes that contained important data in relation to implantation. Saggital, parasaggital and coronary reconstructive images were made at the areas corresponding to the implants planned. Bone supplies were measured. Bone density was determined by high lighting technique.

4. Bone size measures:

Mandibular resections performed for various etiological reasons and differing in size require to determine the size of the mandibular segment to be resected as well as the size of the graft to be obtained during reconstructive surgery before the intervention. Measurements were done on the size of the mandibula and the spina capula bone obtained by trapezius OMC lobe.

3 measures important in relation to the reconstruction were taken on the mandibula:

I. the size of the ramus from the processus condylaris to the angulus mandibulae

II. the size of the corpus from the angulus mandibulae to the protuberancia mentalis

III. the distance between the processus condylaris and the protuberancia mentalis

For the measurement of the scapula the following measures were taken:

I. Determination of the height of the scapula by measuring the distance between the angulus superior and the angulus inferior

II. Determination of the width of the scapula between the boundary of the superior and median thirds of the margo medialis (where the spina scapulae originates in a low, triangle shape) and the furthest point of the acromion.

III. Determination of graft length by measuring the distance between the spina scapulae, where its width was at least 10mm and the acromion where it was at least 2 cm thick.

The measures and their statistical analysis are shown in the Tables.

5. Surgical interventions

The most frequently used appliance in prosthetic dentistry is bridge. Of the permanent teeth, it is the first molars that erupt first during human development. Since it occurs at the age of 6, when oral hygiene cannot be properly ensured, tooth loss is frequent as a result of early caries. Third molars often remain embedded in the jaw bones or do not develop at all. If the second molar is lost too, the only possibility for the fixed substitution of posterior tooth loss is implantation or dentoosseal autotransplantation in the upper jaw.

We examined its effect on the parodontium in animal experiments.

5.1 Dentoosseal autotransplantation

The crown of the tooth to be transplanted is prepared: metal caps are placed on it as well as on the anterior pillar tooth; the tooth root is filled. The premolar is circumscribed with a fine drill so that the root from the processus alveolaris should be covered by an at least 1-1,5 mm thick bone. Then the recipient bedding is formed in a way that the sinus mucosa is lifted and the

bones with the tooth are inserted in the opening. The wound is closed. After placing the caps on the teeth, casting is taken. The technician connects the two crowns with a bar. The teeth are fixed with the help of this bar.

For the substitution of extensive tissue deficiencies the following reconstructive methods were used:

5.2. Pectoralis major muscolocutanous lobe (PMMC). The lobe was prepared by the method described by Ariyan (1979).

5.3. Latissimus dorsi musculocutaneous lobe (LDMC). The lobe was prepared by the method described by Tansini (1906) but was rotated into the defect by the method described by Knyeres (1981).

5.4. Trapezius osteomusculocutaneous lobe (OMC). The lobe was prepared by the method described by Pamje and Cutting (1980).

5.5. Preparation of radial forearm lobe. The extraction of the lobe first described in China was done by the method described by Barabás and Szabó (1993).

5.6. Preparatin of jeujunal lobe done by the method of Reuter et al. (1980).

6. Analysis of antibiotic therapy:

Antibiotics are used for prophylactic and therapeutic purposes in the case of orofacial infections, traumas and tumour surgery. Among the microbes causing the inflammation of the region, aerobe and anaerobe bacteria can be found. For the evaluation of the antimicrobial effect it is essential to know the secretion degree of the given antibiotic in the saliva and blood, i.e., how effective of this double offensive will be. For the assessment of these parameters, serum and saliva levels of cefoxitin (Mefoxin, MSD), a beta lactamase with a stable, enhanced anti anaerob effect belonging to the second generation of cephalosporins were measured. Cefoxitin was administered in a dosage of 3x2g iv to the patients (n=10, 6 males and 4 females) for 4 days. Mixed saliva and

blood samples were collected half an hour after the administration, then every hour (through 6 hours). The antibiotic concentration of the samples was measured by the methods described by Grove and Randal (1955) and the in vitro agar diffusion method by Uri (1956). Bacillus subtilis spore suspension was used as a test bacterium. Antibiotic concentration of serum and blood was measured by extrapolation. Statistical analysis was done by Student's two sample t-test.

We also analysed antibiotic utilisation at the Unit of Oral Surgery of the Department of Stomatology between 1989-1998. This had to be done because the understanding of antibiotic pharmacokinetics is only - though important - part of the treatment of infections. Resistance development, the use of new drugs require continuous quantitative and economic analysis of antibiotic use. We analysed the number of patients treated by antibiotics, total number of patients, duration of treatment and the number of days with fever. The selected antibiotics (whose employment was decided empirically or targeted when in the possession of **harvest** results) were set. The results were grouped according to the use for the five most frequent diseases: fractures, abscesses, cysts, periostitises and chronic sinusitises with antroalveolar fistulas.

Results:

1. Measurement of reactive oxygen intermediaries and environmental effects on inflammations:

1.1.Measurement of reactive oxygen intermediaries:

At the beginning of phagocytosis, the oxygen consumption of the cells increases and reactive oxygen intermediaries (ROI) are produced These free radicals have an antimicrobial effect but on leaving the cells they cause serious damage to the surrounding tissues.

As a result of lipid peroxidation due to the ROI – membrane interaction, malondialdehyde (MDA) is produced. We found its protein level was elevated in

the granulomatous tissue. In accordance with this finding, glutathion peroxidase (GSH-PX) (which has an antioxidant effect) activity was significantly lower than in the control sample. However, it is interesting to note that the activity of superoxide dismutase (SOD) (which also has an antioxidant effect) was the same as that of the control tissues.

1.2. The relationship between weather fronts and surgical interventions, tooth extractions, inflammations requiring incision was confirmed by the analysis of data at the outpatient clinic of the Unit of Oral Surgery. Abscess incision showed a close relationship with warm fronts and cyclones. The negative results of the critical correlation coefficient "r" (n1=60, n2=179) in cold fronts and cyclones show that incision, as an indicator of inflammation activity decreases with the frequency of the above weather events. The number of incisions shows a significant correlation with warm fronts.

2. Histological analysis of the transplant:

The rate of successful operations was 70% in laboratory animals. In order to get the best results, the histological development of the transplant was followed up on laboratory animals.

2.1. After haematoxyin-chromotrop dying, light microscopic examination found the thickness of both cellular and acellular cement layers normal. The width of the periodontal gap of the transplanted teeth did not show significant differences from that of the control teeth. The main run of the collagen fibers and their insertion into the cement and bones could be clearly seen. No significant differences were observed between the structure of the periodontum of the transplanted tooth and that of the control. The main runs of the fibers between the transplanted tooth and those of the control were the same. On the periodontum next to the bone of the transplanted teeth, among the collagen fibers parallel to the alveolar bone wall, fibroblasts and blood vessels could be discerned. In the alveolar corticalis, osteons could be seen with the Havers channels situated in the middle. In the lacunas, osteocytes

with normally dying nuclei could be detected. The entry of the periodontal collagen fibers into the bone could be well discerned and followed into the bone as Sharpey fibers.

2.2.Topo-optical reactions:

A collagen specific topo-optical method was used for the examination of the base material of connective tissues. Path distance was measured by Reichert-Zetopon polarised microscopy in neochromatic light with N4 compensator after Picrosirius red 3B staining, which is an additive topo-optical reaction. A double cleavage of average strength was found in the cement of both the transplanted and control teeth. The arrangement and orientation of the collagen were stable following the transplantation, which was confirmed by the path distances measured. No significant alteration was found between the two samples. The circular polarization of the Haversian lamellae was firm. The intensity of the double cleavage was stronger as related to the cement and weaker than that of the periodontium, which was confirmed by the path distances measured. No significant alteration was found in the ratio of double cleavage in the bones surrounding the control and transplanted tooth. The histologic structure of the transplant was preserved, which justifies the technique employed.

3. **Computer tomography examinations:**
4. In the preparatory phase of transplantation, computer tomography (CT) examinations were performed on the patients in order to measure the structure of the mandible, the running of the canalis mandibulae and to compare the findings with traditional X-ray pictures. The saggital, parasaggital reconstructive pictures taken from the axial slices well discern the shape of the maxilla processus alveolaris in the given plane and the software permits the measurement of bones at any place. In coronary plane reconstructions the sinus base can be well detected in the molar zones. The most suitable place for inplantation can be selected, the quantity of the

osteoplastic material estimated. The bone selection needed for primary stability can be measured precisely. The result of the interventions, e.g., sinus filling, osteoplasty can be judged. Thus CT examination provides much more information than traditional x-ray examinations.

5. Results of measures on dry bones:

Mandibular resections anticipate the need to determine the size of the mandibular segment and estimate the proportions of the graft prior to the intervention. We performed a series of measurements to determine the size of the mandible, and the spina scapulae gained by trapezius OMC lobe. According to the measurements, the average size of the mandibular rumus was 47,5 mm. The average length of the corpus mandibulae proved to be 88,4 mm. The follow up examination of the patients of the Unit of Oral Surgery revealed that the size of the mandibular segment removed by complex surgical interventions ranged between 40-90 mm.

The average height of the scapulae was found to be 149,7 mm. The size of the bone bar gained from the spina scapula - before the acromion were thinned as much as to risk bone fracture or damage shoulder joint movement - was 88,7 mm. In 2 cases we were unable to get an optimal size though the scapula was of normal or larger size. A smaller than average size scapulae did not, however, mean that we could not get an appropriate size bone bar from the spina scapulae. These experiences greatly helped us in planning reconstructive surgery and improved the efficacy of interventions.

6. Results of the surgical interventions:

We performed dentoosseal autotransplantation on humans in seven cases. Out of these 1 tooth was lost five years after the operation.

79 PMCC, 19 trapezius OMC, 5 LDMC lobes were used as pedicle lobes and 8 radial forearm lobes, 1 latissimus dorsi and 1 jejunum lobe were transplanted by microsurgery. The ratio of complications corresponded to that of the literature. Per primam wound healing occured in 78 cases (69,6%), side necrosis in 16 cases (14,3%), partial skin necrosis in 12 (10,7%) and complete skin necrosis in 3 cases (2,7%). Complete lobe necrosis hindered wound healing in 3 cases (2,7%). The most frequently used substitution was PMMC lobe, then trapezius OMC and LDMC. Radial forearm lobe was used for face substitution and after hemiglossectomia. Jejunum was used in 1 case for mucosa substitution in a case of serious intraoral burning.

6.Notes on the secretion of antibiotics in saliva and their use in oral surgery

Antibiotics are used in the infections and surgery of the orofacial region for prophylactic and therapeutic purposes. It is essential to know in what extent a given antibiotic is secreted in the saliva and blood, i.e., how effective the double target point (blood and saliva) is. Cefatonin in iv. 2 g reached its top (4,6± 0,8ug/ml)in the serum half an hour after the administration and six hours later it was low (0,8±u0,1g/ml). In the saliva, the top (1,1±0,0ug/ml) was measured after 1 hour, which is the quarter of that of the blood and was very low (0,2±0,07ug/ml) in the third hour.

5011 patients were admitted to our unit in the period studied, out of these antibiotics were employed in 2075 cases (41,4%). Drug use relatively decreased and duration of treatment became shorter. Cultured samples showed that the most frequent pathogenic agents were coagulase negative Staphylococcus and a-haemolytic Streptococcus. Kleibsiella, Pseudomonas, Enterobacter were less frequent. In fractures, the following antibiotics were used in that order: Augmentin, Aktil, Dalacin; in abscesses, Augmentin, Dalacin, Aktil; in cysts,

Augmentin, Aktil, dalacin; in periostitis, Augmentin was mostly used, in antroalveolar fistulas and chronic sinusitis, Augmentin, Aktil, Ciprobay.

Discussion

The tissue structures in the oral cavity and in its neighbourhood can be easily injured. Dental caries and consecutive acute and chronic inflammations may cause different tissue damages and result in tooth loss. Excessive smoking and drinking have increased the rate of mortality from oral neoplasms fivefold in Hungary in the past decades. The only solution to both problems is prevention. Oral hygiene, improvement of oral health status, moderation of smoking and drinking would decrease the number of carieses and neoplastic diseases. If there is no improvement in the primary and secondary prevention of these diseases, an ever growing number of inflammations and their sequels as well as neoplastic diseases will have to be treated with the methods available today.

Our investigations have confirmed that reactive oxygen intermediaries may be responsible for the tissue destruction in the defence mechanism of the often symptom-free periapical lesion. The human organism living with an inflammation may adversely react to an environmental change that a healthy organism does not perceive. Simple events, like weather changes, weather fronts may overthrow the balance and induce surgical intervention or tooth removal. With an increase in the number of lost teeth, the masticatory apparatus cannot ensure proper chewing of the food, which leads to digestive disturbances. Prosthetic dentistry provides several solutions for the substitution of lost teeth but most of these devices are removable. The majority of patients feel averse to this solution and are ready to undergo surgical interventions in order to get a fixed prosthesis. A permanent state of toothlessness induces an absorption process that after some time surgeries supporting fixed prostheses can only be performed with difficulty.

Without precise information on the conditions of the jaw bones surgical planning may lead to complications, so CT examinations (routinely used in other fields of medicine) – were introduced in dental diagnosis. The method of dentoosseal transplantation as an alternative to expensive implantation was also elaborated at our unit. The survival of the periodontium was confirmed experimentally by this method..

The surgery of malign oral neoplasms should always be supplemented by restorative surgery. Out of the 2000 newly admitted patients with oral neoplasms in Hungary per year, about 200 are in our region and only half of them are in a state suitable for surgery at the detection of the disease. For patients with II-IV stage neoplasms, the chances for survival with a proper quality of life can only be ensured by a complex and correct oncologic and restorative therapy. To achieve this purpose, we introduced several techniques that have become routine methods for now. The number of reconstructive surgeries has stabilised in the past few years and the need has arisen to employ techniques that provide better functional results.

In the majority of cases, maxillofacial surgery is performed in strongly infected areas. Most surgical interventions are accompanied by bacterial infections which may endanger the surgical outcome, lengthen the duration of recovery through complications and thus resulting in economic drawbacks. The bacterial flora of the oral cavity as well as the most frequent agents should be well known by the surgeon. It is essential to select the first antibiotic to be employed with care since the result of the cultures will be known only days later. It is best to use double target antibiotics that achieve high concentration both in blood and saliva.

Conclusions

The quantity of reactive oxygen intermediaries is elevated in periapical granuloma and is considered to be responsible for tissue damages.
Weather changes, especially hot fronts may provoke chronic inflammations.
The tooth transplanted together with the bone is suitable for tooth substitution.
The periodontum reacts to the transplantation with small alterations. The surgical support of dental prostheses is a valuable solution if strict indications are kept.
The use of CT greatly improves the quantity and quality of infromation gained through preimplantologic diagnosis. The most important parameters of the severely resorbed jaw bones may be best assessed by CT.
At best, a 80-90 mm bone graft can be obtained from the scapular spine for reconstructive purposes.
Treatment of advanced oral neoplasms can only be achieved if accompanied by reconstruction. Research is done on techniques providing better functionality and on solutions with higher tissue integration.
With the use of antibiotics, the administration of preparations secreted in high concentration in saliva is suggested (double target).

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