**Oral Diseases (2007) 13**, 206–213. doi:10.1111/j.1601-0825.2006.01268.x

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## ORIGINAL ARTICLE

# Electrostimulating device in the management of xerostomia

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**INTRODUCTION: The present study was undertaken to evaluate the safety and effectiveness of a recently developed electrostimulating device mounted on an individualized intra-oral removable appliance.**

**MATERIALS AND METHODS: The device, containing electrodes, a wetness sensor, an electronic circuit and a power source, was tested on patients with xerostomia in a crossover, randomized, sham-controlled, double-blinded, multicenter study. Electrical stimulation and also sham were delivered during 10 min to the oral mucosa, in the mandibular third molar region. Oral dryness was measured by the sensor. As the primary outcome, sensor dryness and xerostomia symptom changes as a result of device wearing were assessed, and compared between active and sham modes. In addition, side-effects were recorded.**

**RESULTS: Electrostimulation resulted in a significant decrease in sensor dryness, leading to a beneficial effect on patients' subjective condition. No significant side-effects were observed.**

*Oral Diseases* (2007) **13**, 206–213

**Keywords:** dry mouth; salivary glands; salivary flow rate; Sjögren's syndrome

## Introduction

Xerostomia is the symptom of oral dryness resulting most frequently, but not exclusively, from salivary gland hypofunction (Fox *et al*, 1985; Sreebny and Valdini, 1988; Grisius, 2001). Its prevalence in the general population is estimated to range between 10% and 29%, more frequently in women than in men (Sreebny and Valdini, 1988; Billings *et al*, 1996; Nederfors *et al*, 1997; Pujol *et al*, 1998), but to be particularly high in older adults, ranging from 14% to 18% (Locker, 1993; Thomson and Williams, 2000; Nayak *et al*, 2004) and from to 27% to 37% in the elderly population (Ben-Aryeh *et al*, 1985; Gilbert *et al*, 1993; Schein *et al*, 1999), thus suggesting that millions of people suffer from dry mouth worldwide. Xerostomia can be due to increased medication usage (Sreebny and Schwartz, 1997), systemic medical disorders (Porter *et al*, 2004) including Sjögren's syndrome (Fox *et al*, 2000), radiotherapy-induced damage to salivary acinar tissue (Henson *et al*, 2001), and psychiatric distress (Bergdahl and Bergdahl, 2000).

If saliva secretion is chronically compromised, functional oral disturbances as well as oral hard and soft tissue changes may occur. Besides difficulties in swallowing, speaking, chewing, and tasting, the oral mucosa might become painful and atrophic, and a higher incidence of caries as well as soft tissue infections may occur. Furthermore, food avoidance, nonabsorption of sublingually placed drugs, and noncompliance with medication may also result (Sreebny and Valdini, 1988). Overall, chronic xerostomia is a distressing condition, which can lead to diminished quality of life, social isolation, and loneliness (Rydholm and Strang, 2002).

Given its high worldwide prevalence, therapeutic approaches to manage xerostomia have a considerable medical and social impact, and should satisfy several requirements, as suggested by the Commission on Oral Health, Research and Epidemiology (CORE) of the Federation Dentaire Internationale (Sreebny *et al*, 1992; Sreebny, 2000). Ideally, stimulation of salivation as well as development of a sustained-acting preparation should be preferred because of the great advantage of providing the benefits of natural saliva and a long-term management modality of the xerostomic patient, who is bound to remain a chronic patient. Nevertheless, none of the several treatment concepts for xerostomia used so far fits these needs. Artificial saliva and saliva substitutes have only a short-term availability for wetting the oral cavity and many patients do not continue with their use and instead choose to rely on the frequent use of water (Epstein and Stevenson-Moore, 1992), which is still the

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Received 24 August 2005; revised 20 December 2005, 19 January 2006, 25 February 2006; accepted 26 February 2006

commonest self-management modality performed by patients. Stimulation of saliva secretion by gustatory or masticatory stimulants, including sugar-free chewing gum, candies, and mints, is only effective during the moments of use and some of these stimulants, such as citric acid-based mouthwashes, may have a demineralizing effect on teeth, and the oral mucosa may be irritated (Sreebny *et al*, 1992). Currently available medications for treatment of xerostomia, the sialogogues pilocarpine and cemiveline, have positive effects, but as they have many contraindications and potentially serious side-effects besides interacting with other medications, their use, especially in elderly multimorbid–multidrug patients (Wolff, 1995; Grisius, 2001; Guijarro-Guijarro *et al*, 2001), should be well evaluated, balancing symptomatic efficacy with adverse effects and the expense of treatment (Taylor, 2003).

As an alternative treatment, augmentation of salivary reflexes through the application of an electrical stimulus to the oral mucosa has been reported to significantly increase salivary flow and alleviate xerostomia-related symptoms in patients with Sjögren's syndrome and after radiotherapy to the head and neck (Weiss *et al*, 1986; Steller *et al*, 1988; Talal *et al*, 1992), without relevant local or systemic side-effects. Therefore, the development and clinical application of a miniature intra-oral device for electrostimulation of salivation mounted on a dental implant would give an appropriate and acceptable solution, easy to handle especially for elderly xerostomia patients, and is currently under investigation by the authors in a multinational polyspecialistic European Commission-funded research project (Saliwell project: http://www.saliwell.org). This patented device (Wolff and Yellin, 1999) has been designed in such a way as to have an autonomous software-regulated stimulatory pattern and a remote control unit to allow individual patient-oriented control of stimulation. In addition to augmenting the salivary reflex, the Saliwell intra-oral device is expected to directly stimulate the efferent neural pathways of submandibular and sublingual glands as well, because the stimulating electrodes are positioned medially in the mandibular third molar region, close to the area where the lingual nerve travels alongside the lingual alveolar plate.

The present study deals with the first step of this project, namely a noninvasive test that was performed to evaluate the safety, feasibility, and efficacy of electrical stimulation of salivation.

## Materials and methods

*Experimental design and preparation*

This clinical investigation was designed as a crossover, randomized, sham-controlled, double-blinded, multicenter trial. The primary endpoints of the study were defined as a significant decrease of sensor dryness and an improvement of xerostomia-related symptoms. These parameters obtained during active electrostimulation were compared with those recorded during sham stimulation by the same device.

Three clinical centers were involved in the clinical trials (Centre for Dental Medicine, Department of Oral Surgery and Dental Radiology, Charité – Universitätsmedizin Berlin, Germany; Section of Oral Medicine, Department of Odontostomatological and Maxillofacial Sciences, Faculty of Medicine, University 'Federico II' of Naples, Italy; Clinic of Oral and Maxillofacial Surgery, Hospital Clínico San Carlos, Madrid, Spain). All developmental work was conducted by the Assuta Hospital, Tel Aviv, Israel; Fraunhofer IBMT, St. Ingbert, Germany; Aran R&D, Caesaria, Israel; Relsoft, Rishon Letzion, Israel; and Valtronic, Les Charbonnières, Switzerland in cooperation with the Centre of Applied Gerontology of the University of Birmingham, UK and Nobel Biocare, Gothenburg, Sweden. Study monitoring was performed by MT Promedt Consulting, St. Ingbert, Germany.

After a positive evaluation by the Freiburg International Ethics Committee (Votum no. 03/1343) as well as by the local ethics committees of the clinical centres, patient identification and recruitment were started consecutively. Patients with xerostomia attending the clinical centres and/or referred by outpatient departments of dental medicine, dermatology as well as rheumatology and clinical immunology, and from private dental practices, were evaluated. After performing anamnesis and clinical examination, patients were included if they met the inclusion criteria (Table 1). The following questions were used to assess mental disease/depression (Whooley *et al*, 1997): (a) During the past month, have you often been bothered by feeling down, depressed or hopeless? (b) During the past

**Table 1** Inclusion and exclusion criteria for the study

| *Inclusion criteria* | *Exclusion criteria* |
|---|---|
| Age >17 years | HIV or active HCV infection |
| Clinical symptoms of xerostomia | Severe systemic diseases |
| At least doubling of stimulated whole saliva flow rate compared with unstimulated saliva flow rate | History of head and neck radiation and graft *vs* host disease |
| | Anticoagulants use |
| | Known allergy to materials used in the investigational device |
| | Known mental disease/depression |
| | Wearing active pacemaker, defibrillator, hearing aid |
| | Pregnancy |
| | Completely edentulous mandible |

month, have you often been bothered by little interest or pleasure in doing things? As the device is designed to stimulate the salivary glands, only patients with demonstrated residual salivary gland function capable of a significant response to stimuli were included. (i.e patients whose salivary flow rate at least doubled after stimulation by paraffin/parafilm chewing, namely those with stimulated whole saliva flow rate being two times or more higher than unstimulated whole saliva flow rate). For this purpose, saliva was collected by expectoration into preweighed tubes. Xerostomia was confirmed by a positive reply to the question: Does your mouth usually feel dry? (Sreebny and Valdini, 1988). The goal was to perform at least 100 experiments to attain acceptable data quantity. Each patient was requested to undergo 10 experiments, but as dropout was expected, recruitment of a minimal number of 20 patients was sought. Patients were thoroughly informed about the aims and course of experiments as well as possible side effects, and written informed consent was obtained.

An impression of the maxilla and mandible of each patient was taken to prepare plaster models. Special attention was given to include the lingual area of the mandibular alveolar ridge corresponding to the second and third molars for proper placement of the electrodes close to the lingual nerve.

*The electrostimulating device*

The electrostimulating device named 'GenNarino' (Beiski and Wolff, 2004) was manufactured for each individual patient. It consists of a custom-fitted tray, similar to those used for topical application of fluoride, upon which the electrical circuitry, the stimulation electrodes, a battery, a wetness sensor, and the remote control receiver were mounted using a sandwich technique (Figure 1). The electrical circuitry consists of a very low-power microprocessor controlling a current source circuit, which is able to generate accurate current pulses. The remote control, via the microprocessor and the transceiver circuit, defines the pulse-train duty cycle to achieve the desired stimulation level. It also contains a software specifically developed to control the electrical parameters of the stimulation, such as amperage, frequency, and pulse width. The stimulation electrodes are connected to the circuitry, and protrude through the tray in order to contact the oral mucosa and deliver electricity.

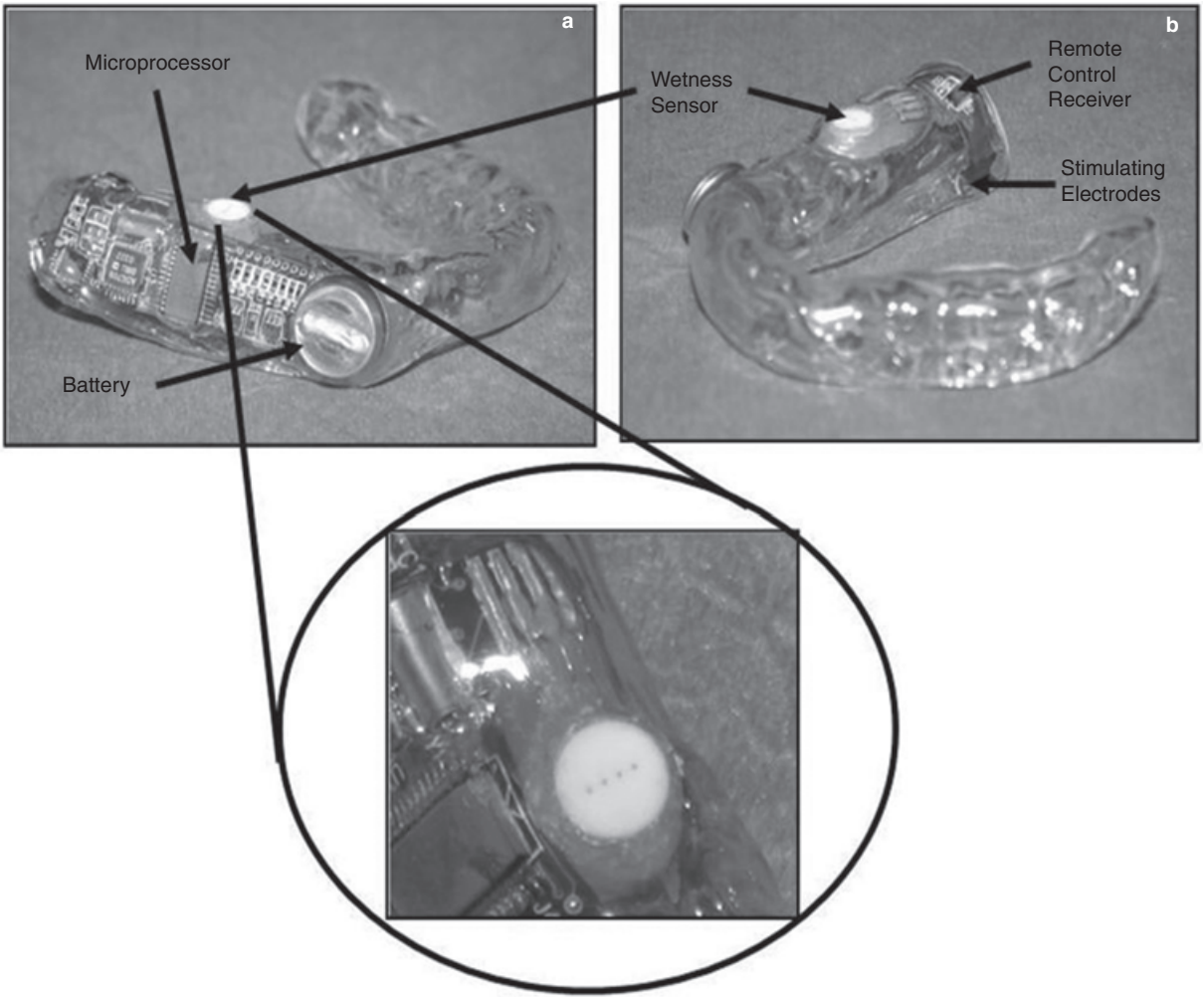


**Figure 1** Right (a) and left (b) view of the GenNarino showing the wetness sensor (magnification), the battery cell, the diode for remote control commands reception, and the remaining electronic components. The stimulating electrodes are located on the lingual side of the third molar area

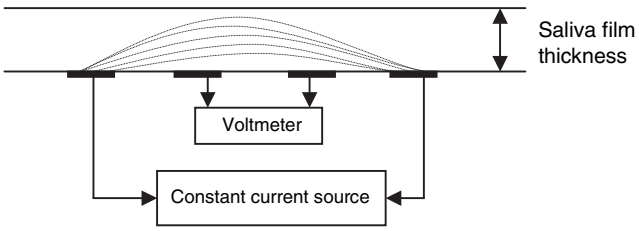


**Figure 2** Principle of the wetness sensing method

The wetness sensor measures the impedance of the salivary film deposited on top of it and acts as a resistor. The impedance of a resistor depends on its geometrical dimensions and thus on its thickness. As the salivary film is used as the resistor, variations in film thickness can be measured as a change in impedance (Vogel, 1997). The principle is based on similar methods used for industrial and biological applications (Nebuya *et al*, 1999; Wenxing *et al*, 2005). Salivary impedance is measured by a four-electrode arrangement. An alternating current with small constant amplitude is passed through the outer two electrodes and the voltage drop is measured between the two inner electrodes. Impedance value is obtained by dividing voltage by current (Figure 2).

*Performance of experiments*

A randomized stimulation schedule, which contained the stimulation pattern for each experiment, was prepared for each patient by the study coordinator. These stimulation parameters were included into the software, and were set for each experiment by commands transmitted from the remote control to the GenNarino prior to its insertion into the patients' mouths. The investigators and the patients were blinded to the stimulation schedule.

The patients were asked not to drink or eat anything, or take any medication or smoke within 90 min prior to each experiment. If two experiments were performed in one day, a resting period of at least 90 min was necessary between the experiments.

Before and after the procedures, blood pressure and heart rate were checked and a visual investigation of the oral mucosa was performed to rule out any lesions and to perform a comparison of its status prior to and after the experiment. Each experiment consisted of one active stimulation test and one sham test (inactive stimulation pattern) in a random order – GenNarino wearing lasting 10 min each in both procedures – with an interval of 35 min (Figure 3). The intervals between the start and stop of GenNarino wearing were determined by a stopwatch. The stimulation (or sham) patterns were set using the remote control. Immediately upon GenNarino insertion into patients' mouth, wetness sensor recording started. Initially, wetness sensor recording was discontinued at minute 5 (5-min experiments), and subsequently at minute 10 (10-min experiments). Finally, patients were asked to compare the results of both experiments in relation to their xerostomia status. The specific question was: Please select the answer that best fits your feeling: (a) the effect of both experiments was similar; (b) the first had a better effect on my dryness or (c) the second had a better effect on my dryness.

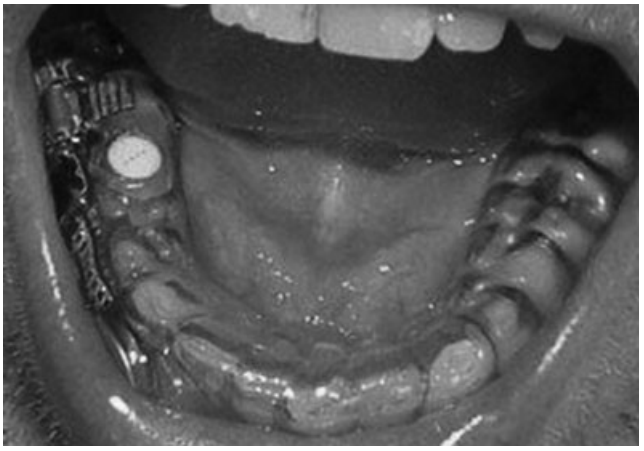

**Figure 3** The GenNarino inside the mouth

*Data recording and statistical evaluation*

All patient data were coded numerically by a patient identification number. The digital signal of the wetness sensor expressed in numbers was used as a measure of dryness, which is expressed by the impedance and is inversely proportional to the thickness of the saliva film. The wetness sensor recorded the dryness status once every minute. The numerical values chosen in the software for 10-min experiments were in a higher range than for 5-min experiments, but this decision has no influence on the relative meaning of the wetness sensor readings, as the numeration was arbitrarily chosen.

Wetness sensor data were transferred from the GenNarino to a personal computer (PC) for further processing. For that purpose, a cable was connected to the device's electrodes to transmit the data to the PC through the serial port. A comparative analysis between sham and active was performed regarding the repeated measures of dryness every minute. Statistical analysis of the data was performed by an independent statistical bureau (Institute for Applied Statistics, Dr Jörg Schnitker GmbH, Bielefeld, Germany), using the statistical analysis system (SAS) system. The statistical tests used were: Crossover design 2-period (Grizzle, 1965), sign test (Dixon and Mood, 1946), *t*-test, and analysis of variance for the repeated-measurement design (Winer, 1971). $P < 0.05$ was considered statistically significant.

## Results

Between October 2003 and March 2005, 158 experiments were performed on 20 women (86.4%) and three men with xerostomia: 10 patients in Berlin, 10 in Madrid, and three in Naples. All patients were Caucasian. The median age of patients was 61.5 years (range 28–79). The baseline salivary flow-rates of the patient categories (Sjögren's syndrome, medication-induced xerostomia, and idiopathic xerostomia) are summarized

**Table 2** Baseline salivary flow-rates of the patient categories

| | | *Unstimulated salivary flow-rate (ml min$^{-1}$)* | | *Stimulated salivary flow-rate (ml min$^{-1}$)* | |
|---|---|---|---|---|---|
| *Diagnosis* | *n* | *Mean* | *s.d.* | *Mean* | *s.d.* |
| Primary Sjögren's syndrome | 10 | 0.07 | 0.08 | 0.72 | 0.65 |
| Medication-induced xerostomia | 7 | 0.13 | 0.14 | 0.55 | 0.38 |
| Idiopathic xerostomia | 6 | 0.11 | 0.06 | 0.49 | 0.10 |

in Table 2. No statistically significant differences were recorded for unstimulated and stimulated flow-rates. In 72.7% of the patients, the use of xerogenic drugs was registered, one patient had salivary gland swelling, two were smokers, three wore removable upper prostheses, and two removable partial lower prostheses.

Pre- *vs* post-procedural changes in blood pressure (BP) and heart rate (HR) were determined as follows: systolic BP decreased from 121.8 ± 19.2 to 119.2 ± 16.3 mmHg ($P < 0.02$); diastolic BP decreased from 72.9 ± 10.9 to 72.4 ± 10.5 mmHg (n.s.); HR decreased from 74.2 ± 10.2 to 68.8 ± 9.8 bpm ($P < 0.0001$). No significant negative side effects were observed during as well as after the experiments. Erythema was observed on the oral mucosa of patients in six of 158 experiments (4%). Five of these lesions occurred in the area of contact with the electrodes. All of them healed uneventfully. Minor adjustments of the device were made to address complaints about pressure on the oral tissue deriving from the protruding electrodes and the vestibular margin of the GenNarino, which were expressed by 19.3% of the patients. Two episodes of short tickling sensation were noted by two patients, but were not described as discomfort. Other negative symptoms were not reported by the patients.

Wetness sensor data were not available from part of the study because of downloading problems from the sensors to the PCs in several experiments, derived from contact difficulties between the transmission cable and GenNarino's electrodes. Table 3 depicts the data

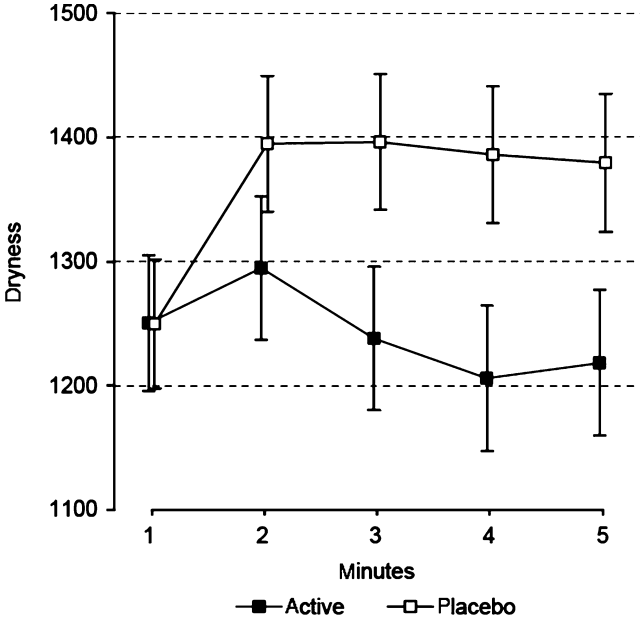


**Figure 4** Mean and s.e.m. values of sensor dryness in the course of 5 min active ($n = 47$) and sham ($n = 52$) stimulation

provided by the wetness sensor in both the 5-min and 10-min experiments, while the course of five repeated measures presented in Figures 4 and 5 shows the corresponding curves over 10 repeated measures. After 1 min of wearing GenNarino, the registered dryness status was similar in sham and active modes. However, after 3 min of the 5-min experiments, significantly lower dryness was seen in the active mode when compared with sham. The superiority of the active mode was expressed by means of a highly significant interaction indicating a different time–effect profile during both treatments: decrease of dryness while GenNarino is active and increase of dryness (compared with the first measurement) during the sham situation. Ten repeated measurements of dryness yielded significant differences after 2 min of the experiment. The resulting significant interaction also resulted in a significant treatment difference.

**Table 3** Dryness measurements by the wetness sensor

| | *5-min experiments* | | | | | *10-min experiments* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *Active ($n = 47$)* | | *Sham ($n = 52$)* | | | *Active ($n = 49$)* | | *Sham ($n = 59$)* | | |
| *Min.* | *LS mean* | *s.e.m.* | *LS mean* | *s.e.m.* | *Comparison active vs sham (t-test; P-value)* | *LS mean* | *s.e.m.* | *LS mean* | *s.e.m.* | *Comparison active vs sham (t-test; P-value)* |
| 1 | 1250.4 | 54.8 | 1249.7 | 52.1 | 0.9926 | 2514.6 | 137.3 | 2441.3 | 125.1 | 0.6942 |
| 2 | 1294.7 | 57.5 | 1394.9 | 54.7 | 0.2098 | 2208.6 | 164.1 | 2753.2 | 149.5 | 0.0158 |
| 3 | 1238.0 | 57.7 | 1396.3 | 54.9 | 0.0497 | 2185.4 | 176.5 | 2801.0 | 160.8 | 0.0113 |
| 4 | 1206.0 | 58.3 | 1386.1 | 55.4 | 0.0274 | 2176.0 | 184.6 | 2834.4 | 168.2 | 0.0096 |
| 5 | 1218.2 | 58.5 | 1379.4 | 55.6 | 0.0487 | 2096.5 | 190.0 | 2890.9 | 173.1 | 0.0025 |
| 6 | | | | | | 2075.0 | 190.3 | 2856.6 | 173.4 | 0.0030 |
| 7 | | | | | | 2150.2 | 192.5 | 2904.5 | 175.4 | 0.0046 |
| 8 | | | | | | 2079.5 | 191.8 | 2940.7 | 174.7 | 0.0012 |
| 9 | | | | | | 2093.8 | 192.1 | 2904.1 | 175.0 | 0.0023 |
| 10 | | | | | | 2166.5 | 190.7 | 2858.4 | 173.8 | 0.0085 |
| | | | ANOVA: $P = 0.0001$ | | | | | ANOVA: $P < 0.0001$ | | |

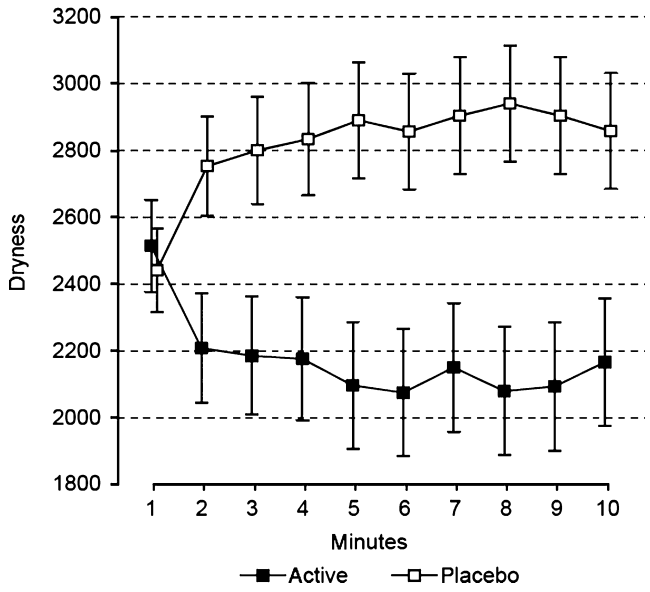


**Figure 5** Mean and s.e.m. values of sensor dryness in the course of 10 min active ($n = 49$) and sham ($n = 59$) stimulation

**Table 4** Comparison of subjective perception of experimental results by the patients, considering the order of the modes – sham and active ($n = 158$)

| *Patients' judgement (first vs second test)* | | | | |
|---|---|---|---|---|
| | *Dissimilar* | | | |
| | | *The chosen test was on…* | | |
| *Similar (%)* | *Preference* | *Sham mode (%)* | *Active mode (%)* | P-*value** |
| 24.1 | First test better | 13.9 | 12.0 | n. s. |
| | Second test better | 16.5 | 33.5 | $P < 0.005$ |

*For sham *vs* active comparison.

As to the subjective preference of active or sham, 38 of 158 (24.1%) experiments yielded no differences between active and sham. In the remaining 120 experiments, the active mode was preferred in 72 cases (60.0%) and sham in 48 cases (40.0%) ($P < 0.05$). When the preferred mode was the first test, there was no significant difference between the sham and active modes. However, the active mode was clearly the preferred mode ($P < 0.005$) when the second test was chosen by the patients as the most effective one (Table 4).

## Discussion

Neural electrostimulation of salivary gland function by application of electrical current, through the oral mucosa, on afferent nerve pathway receptors has been reported to increase production of saliva and to reduce the symptoms of xerostomia because of several conditions (Weiss *et al*, 1986; Steller *et al*, 1988; Talal *et al*, 1992). It is believed that afferent nerves carry such impulses to the salivary nuclei (salivation center) in the medulla oblongata which in turn directs signals to the efferent part of the reflex leading to initiation of salivation. More recently, the use of extra-oral transcutaneous electric nerve stimulation (TENS) over the parotid gland was reported to effectively increase saliva production in healthy individuals, suggesting that TENS might directly stimulate the auriculotemporal nerve that supplies secretomotor drive to the parotid gland (Hargitai *et al*, 2005). Saliwell project is aimed at implementing the salivary electrostimulation concept, developing a miniature intra-oral device mounted on a dental implant, capable of continuous auto-regulated stimulation and also controlled by a remote control.

In a first step of this project, data concerning increase in salivation and symptom relief after electrical stimulation of the lingual area of the mandibular third molar region, close to the lingual nerve path, were obtained using a removable device in a non-invasive test. Due to the novelty of the approach that intimidated potential candidates to participate in the study, patient recruitment was rather slow. However, no significant negative side effects have been recorded during and after the experiments. Complaints of discomfort have easily been solved with adjustments made to the electrodes and flanges. Erythematous changes of the tissue in contact with the electrodes were rare thus signifying no limitation to the use of the device.

Previous studies have demonstrated that the assessment of salivary film thickness covering oral surfaces might be more appropriate for diagnosing dry mouth, as it is a direct measurement of wetness of the mucosal tissues and identifies those who perceive dryness but are not considered to be hyposalivators because of resting salivary flow $>0.1$–$0.2$ ml min$^{-1}$ (Wolff and Kleinberg, 1998; Kleinberg *et al*, 2002). Collins and Dawes (1987) calculated that if saliva was evenly distributed throughout the mouth, it would present as a thin film of 72 and 100 $\mu$m thickness after and before swallowing, respectively, between two opposing surfaces of the mouth in contact. While the traditional method of oral wetness/salivary film thickness determination requires the use of filter papers (Sialopaper™ and Ora Flow® strips) and electronic micromoisture meters (Periotron 8000® and Ora Flow®; Wolff and Kleinberg, 1998), the Saliwell Study Group developed and validated such an electronic sensor *in vitro* to obtain real-time recording of wetness changes during stimulation. Traditional salivary collection methods were impractical because of the presence of the GenNarino device in the mouth. In addition, these methods do not assess the total fluid output, but rather the net output of saliva after loss of fluid by evaporation and/or by mucosal absorption (Dawes, 2004). Despite the technical difficulties in downloading sensor data experienced in some experiments, the data were statistically adequate. The goal of sensor readings transmission to the PC was to obtain data for the present study. Thus, the problems experienced in this procedure during the study have no significance for the routine clinical use of the GenNarino device.

The first wetness sensor signals were elicited after 1 min of GenNarino wearing and their intensity was similar in sham and active modes, probably because of acute stimulation of mucosal mechanoreceptors by the device itself. However, thereafter, a gradual differentiation process between the sham and the active modes evolved. In fact, a significant decrease of sensor dryness was detected because of the intra-oral presence of the GenNarino on active mode, as opposed to the effect of the sham device. It is known that the presence of an intra-oral foreign body such as a complete denture *per se* acts as a mechanical stimulus in the salivary reflexes, initially augmenting secretion, followed by a return to baseline because of adaptation (Jensen *et al*, 1991; Wolff *et al*, 2004). As a consequence, the increase in dryness after the first minute of the wearing of the sham GenNarino (relative to the first measurement) can be explained by the adaptation process of salivary glands to the presence of a foreign body. On the contrary, the decrease in sensor dryness registered during the presence of the active GenNarino mode implies that electrical stimulation overcomes the adaptation process of salivary glands.

The present study also shows patient preference of the active GenNarino mode over the sham mode among the second tests, when they were selected as the most effective modes in relieving xerostomia. However, almost one-third of patients (30.4%) reported the sham mode to be more effective than the active mode. We think that the acute effect of mechanical stimulation might have confounded the subjective evaluation of oral wetness. As previously described, each experiment consisted of a sham and an active test, the order of which was not known to both patients and clinicians. Patient memory could play a role in the selection, as more patients chose the second test (50%) over the first one (25.9%). Consequently, the ability of the patients to choose active over sham was greater, the closer the test was to the moment of their decision.

Use of the GenNarino device as a routine treatment of patients with xerostomia may be bound by very few (if any) contraindications. Several patients groups were excluded from the study (Table 1). However, they may not constitute an absolute contraindication for using a GenNarino device. Professional pre-assessment is warranted for certain potential users, such as patients with pacemakers or defibrillators (by a cardiologist) or hearing aids [by an ear, nose and throat (ENT) specialist] and psychiatric patients (by a psychiatrist). Pacemakers have built-in safety features to protect them from interference from other electrical devices that may disrupt their operation. Similar to the concomitant use of cochlear implants and pacemakers, which were found to be compatible with absolutely no interference (Triglia *et al*, 1996; Huang *et al*, 1999; Rebscher *et al*, 1999), the GenNarino can also be used alongside other wearable electronic devices.

In summary, the salivary glands of patients with xerostomia showed a good response to electrostimulation by the GenNarino device. This also had a beneficial effect on the patients' subjective condition. The results are encouraging to continue with the Saliwell project toward the next steps of developing and investigating the miniature electrostimulating device mounted on a dental implant. This device, which will stay permanently in patients' mouths, will chronically apply electric stimulation, thus possibly leading to constant and lasting salivation with a significant impact on the patients' quality of life.

## Acknowledgements

The Saliwell research project was supported by the European Commission under the Fifth Framework [Project: Saliwell Information Society Technologies (IST) 2001-37409]. The Saliwell clinical team is thankful to the Saliwell Research and Development team including: O Steinmetz, KP Koch, T Velten, O Scholz (Fraunhofer Institute, St. Ingbert, Germany), M Rinck (Promedt Consulting, St. Ingbert, Germany), L Nayak (University of Birmingham, UK), S Kolly, P Clot (Valtronic, Les Charbonnières, Switzerland) and BZ Beiski (Saliwell Ltd, Assuta Hospital, Tel Aviv, Israel).

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