Institution: King's College London

Unit of Assessment: UoA3 - Dental

Title of case study: Revolutionising treatment of salivary gland obstructive disease

1. Summary of the impact

In the last two decades researchers at King's College London (KCL) have revolutionized the management of benign surgical salivary disease (obstruction and tumours). Understanding the pathophysiology of the salivary glands has translated into a complete change of treatment away from traditional gland removal to minimally invasive gland preserving management. In obstructive disease >90% of stones can be released and <3% of glands removed. Similarly most parotid tumours can be removed safely by extracapsular dissection preserving the gland and significantly reducing risk of facial nerve injury. In children, >80% of childhood ranulas now can be treated without sublingual gland removal. KCL's Dental Institute has become a UK referral centre for minimally invasive salivary procedures and the procedures are now used worldwide.

2. Underpinning research

Each year, approximately 59 million people worldwide develop obstructive salivary gland disease (OSGD) primarily as a result of salivary stones, salivary gland duct strictures, mucocoeles, salivary cysts and ranulas. Of these, twenty million people a year are admitted for strictures, accounting for around 23% of operations for benign salivary obstruction. With an average 3 days hospitalisation, annual costs for treatment near £4m. Traditional treatment of OSGD is total sialadenectomy (gland removal), which may bring temporary or permanent nerve injury, haemorrhage, gustatory sweating and an unsightly scar and depression. Alternative, minimally invasive treatment (MIT) has been developed at King's College London (KCL) by Prof Mark McGurk (1988-present, Professor of Oral and Maxillofacial Surgery), Dr Jacqueline Brown (1989-present, Consultant Dental Radiologist) and Dr Michael Escudier (1993-present, Senior Lecturer in Oral Medicine).

Innovative New Approaches: KCL's minimally invasive salivary service developed from many years of investigation into salivary disease pathophysiology and lithotripsy, reported in a large number of studies. For instance, a prospective randomized trial of 142 salivary stones treated with extracorporeal shock wave lithotripsy demonstrated success in over 46% of the cases. A further 34.5% were partial successful with effectiveness dependant mainly on stone size (1). This success prompted development of micro-endoscope and radiological techniques to retrieve small stones with wire baskets and approaches to dilate strictures with balloons. These innovations transformed treatment; need for hospitalization was eliminated for the many of patients, thus reducing costs. However, only stones less than 5mm in diameter could be drawn down the duct and over 50% of parotid or submandibular gland stones are over 5mm. This prompted development of new minimally invasive endoscopic-guided surgery techniques. Salivary stone extraction using a minimally invasive wire basket, radiologically-guided approach under local anesthesia was used in 86 cases. Here, total stone removal was possible in 64% of the patients, partial removal in 14%, with 22% not being removed, most often due to fixation of the stone within the duct. Review at a mean of 17 months showed 82% of the partial or complete removal cases reported symptom relief (2).

Clinical Success: Success of these techniques has been validated by clinical observation and patient-directed review. In one study, out of 186 patients undergoing transoral stone removal only one was unsuccessful at the time and seven had to have further sialadenectomy for persisting symptoms (3). In another, 70 patients underwent endoscope-assisted MIT for parotid stones as an alternate to adenectomy. After an average follow-up of 25.5 months only three had any long-term complications (persistent stone fragment, obstructive symptoms due to a fibrous stricture, visible scarring) (4). Importantly, both these studies reported a low incidence of side effects, one of the major factors in complete gland removal. In the former, only 6% reported a mild tingling, with none reporting the lingual nerve anaesthesia that can occur with sialadenectomy; in the latter, there were no cases of facial nerve weakness or salivary fistula and only one patient reported a visible scar.

Success was initially met with skepticism by peers but a physiology research program in animals and humans demonstrated capacity for substantial gland recovery, as evidenced by a KCL-led European collaborative study looking at long-term outcome of intraoral removal of 118 large

(>10mm) submandibular gland stones. Full (87.3%) or partial (11.9%) removal was achieved for all but one case and after a mean follow-up of 42 months; the majority remained asymptomatic (85.6%), 14.4% had only modest obstructive or infective symptoms and only 3.4% cases suffered recurrent stones. This suggests that the majority of large submandibular gland stones can be removed by gland-preserving procedures retaining an asymptomatic salivary gland. Further, it casts doubt on the premise that salivary stones normally lead to chronic sialoadenitis, former justification for the policy of sialoadenectomy (5). To support MIT, a five-center KCL-led European study of 4,691 cases treated by lithotripsy, endoscopy, basket retrieval and/or surgery found that full or partial clearance was accomplished in 80.5% and 16.7% respectively, with only 2.9% having to undergo sialadenectomy (6).

Spin-Offs: The MIT approach further evolved into new techniques for treating duct strictures and salivary ranulas without surgery. Usual duct stricture treatment, adenectomy, is intrusive and risks neurologic damage and cosmetic deformity. Instead, with balloon dilation under fluoroscopic control in 33 patients, stricture elimination was completely or partially demonstrated in 82% and 14% respectively. At an average follow-up of 6.8 months, of 25 glands examined, 12 were asymptomatic, 12 had reduced symptoms and only one failed to improve. Even where stricture recurred, symptomatic improvement was maintained in the majority of cases (7). MIT has also been used for benign parotid tumours. Historically, treatment was with superficial parotidectomy as it was thought that recurrence could occur if the parotid capsule was left. MIT with extracapsular dissection showed otherwise, as demonstrated in a KCL study of 156 patients. Hospital stay was usually 24 hours or day surgery. As little or no parotid tissue is removed, MIT almost eliminates the risk of Frey syndrome (redness, sweating, pain, numbness) and preserves the face contour. Injury to the greater auricular nerve cannot always be avoided, but the nerve can be preserved in about 60% (8).

3. References to the research

1. Escudier MP, Brown JE, Putcha V, Capaccio P, McGurk M. Factors influencing the outcome of extracorporeal shock wave lithotripsy in the management of salivary calculi. Laryngoscope 2010;120(8):1545-9. Doi: 10.1002/lary.21000 (4 Scopus citations)
2. Brown JE, Drage N, Escudier M, Wilson RF, McGurk M. Minimally invasive radiologically-guided intervention for the treatment of salivary calculi. Cardiovasc Intervent Radiol 2002; 25:352-5. Doi: 10.1007/s00270-002-1950-9 (12 Scopus citations)
3. Coombes J, Karavidas K, McGurk M. Intraoral removal of proximal submandibular stones - an alternative to sialadenectomy? International J of Oral & Maxillofacial Surgery.2009;38:813-816. Doi: 10.1016/j.ijom.2009.02.026 (5 Scopus citations)
4. Karavidas K, Nahlieli O, Fritsch M, McGurk M. Minimal surgery for parotid stones: a 7-year endoscopic experience. Int J Oral Maxillofac Surg 2010 ;39(1):1-4. Doi: 10.1016/j.ijom.2009.06.030 (4 Scopus citations)
5. Zhang L, Escudier M, Brown J, Capaccio P, Pignataro L, McGurk M. Long-term outcome after intraoral removal of large submandibular calculi. Laryngoscope 2010: 120(5): 964-6). Doi: 10.1002/lary.20839 (7 Scopus citations)
6. Iro H, Zenk J, Escudier MP, Nahlilie O, Capaccio P, Katz P, Brown J, McGurk M. Outcome of minimally invasive management of salivary calculi in 4,691 patients. Laryngoscope 2009, 119(2):263-8. Doi: 10.1002/lary.20008 (54 Scopus citations)
7. Drage N, Brown J, Escudier M, McGurk M. Balloon dilatation of salivary duct strictures - report on 36 treated glands. Cardiovasc Intervent Radiol 2002;25:356-9. Doi: 10.1007/s00270-002-1951-8 (11 Scopus citations)
8. George KS, McGurk M. Extracapsular dissection--minimal resection for benign parotid tumours. Br J Oral Maxillofac Surg 2011;49(6):451-4. Doi: 10.1016/j.bjoms.2010.10.005 (9 Scopus citations)

Grants

- Minimally invasive treatment of salivary glands has received a number of grants for equipment from NHS capital bids (2008) as well as Guy's Charitable Foundation and British Association of Oral & Maxillofacial Surgery funding as outlined below:
  - 1996: Mini-lith SL1 (Storz): £80K
  - 2008: New Mini-lith SLi (Storz), £98.4K; Endoscopy stack and headlight, £61.3K; 8

endoscopes, £8K
    - 2009: Ultrasound imager; £80K; Cephalometric Planmeca Promax Direct Digital Dental Panoramic Tomographic & Cephalometric Imaging System imaging system, £75K; Dental Radiology – Agfa CR30, £35K
- South Thames Research Training Fellowship, 1996-1998: £78K. Recipient Dr M Escudier.
- Saudi Government PhD funding, 2000-2004: £70K. Recipients: Proctor and McGurk. Use of saliva as a monitor of recovery from ductal obstruction
- Dental Institutive PhD studentship funding, 2006-2009: £60K: Recipients: Carpenter and Proctor. Rat submandibular gland regeneration following duct-ligation induced atrophy

4. Details of the impact

New Centre to Preserve Glands

Research on minimally invasive treatment (MIT) carried out by the team at King's College London (KCL) led to the setting up of a dedicated MIT Salivary Gland Centre at Guy's Hospital/King's Dental Institute (GH/KDI), London in the late 1990's to capitalize on the innovations in treatment to preserve tissue and reduce trauma (1a-c). The Centre, highlighted in national media including a 2010 article in the Daily Mail (1d), draws approximately 14% of the 3500 people/year across the United Kingdom undergoing treatment for obstructive salivary gland disease (OSGD). Before the KCL-led innovations in treatment, all patients required sialoadenectomy. By in 2011 only 1 of 490 cases treated at GH/KDI required this type of surgery with the rest undergoing MIT. Along with treatment of salivary stones, MIT is also utilised for duct strictures (23% of the 3500 cases of OSGD a year), benign parotid tumours and the much rarer occurrence of salivary ranulas. Both duct strictures, managed by balloon dilation (an average of 59 cases/year), and ranulas, managed by minimal excision preserving the sublingual gland, are now treated in the outpatient setting. As ranulae can afflict young children, this is a significant advance in treatment of such, significantly reducing damage to developing tissues and likelihood of scarring (1c).

Improved Patient Outcomes

Prior to the development of MIT, the standard management of symptomatic stones and parotid tumours was gland removal (sialoadenectomy). This can cause permanent nerve injury in 1.4-3.3% of cases and haemorrhage in up to 14% of operations. In the parotid gland, complications are more profound as the main risk is to the facial nerve and facial animation: permanent injury occurs in up to 4%, temporary injury in 30-60% of cases. Additionally, many patients develop Frey's syndrome (gustatory sweating) and have temporary or permanent anaesthesia of the cheek skin and earlobe. Finally an unsightly depression can occur behind the angle of the mandible due to the loss of parotid tissue. These are nearly all avoided or minimalised by MIT. Another advantage of MIT is that sialoadenectomy is undertaken under general anaesthesia on an inpatient basis, with an average hospital stay of 3 days. MIT has shifted treatment into the outpatient setting for small stones and strictures to day-case surgery for large stones and from a 3-night to a 1-night stay for benign parotid tumours. Thus the development of MIT has not only significantly reduced morbidity of treatment for the patient, but also greatly reduced costs of treatment for the NHS. GH/KDI is a supra-regional referral centre for general MIT and a national referral centre for lithotripsy for England and Wales. As GH/KDI is a supra-regional referral centre for general MIT and a national referral centre for lithotripsy for England and Wales, significant income of £250K in 2008-11 was generated by the provision of these type of procedures (1c).

Educating Clinicians Around the World

KCL researchers use a number of avenues to disseminate their work on MIT and pass on their skills. GH/KDI offers an international training course on MIT, attended by 12 consultants per year with specialities in oral and maxillofacial surgery, ENT and radiology. Prof McGurk, alongside European colleagues, runs similar courses once a year in Paris, France and Erlangen, Germany and together they set up the Second International Conference on Controversies in Management of Salivary Gland Disease in Paris in 2008 for both dissemination of study results and practical, hands-on, teaching of MIT (2). The GH/KDI Centre is also part of the wider London Salivary Gland Centre, run by Prof McGurk, which encompasses both NHS and private practice (3). The work of KCL researchers is the only such cited in the European Association of Oral Medicine's handbook chapter on Obstructive Salivary Disease, with references including Drage 2002 and Escudier 2003

(4). It is also widely utilised in the recently-published clinical handbook 'Controversies in the Management of Salivary Gland Disease', co-edited by Prof McGurk, aimed at oral surgeons and nominated for a 2013 British Medical Association award (5).

Minimally invasive salivary techniques are slowly being adopted throughout the world with an increasing list of publications from Europe, USA and China. For instance, Dr David Eisele at Johns Hopkins Hospital was one of the first surgeons to bring the technique to the USA following observation of the successes of MIT in Europe (6). Additionally, a number of reviews of MIT cite KCL work as being influential papers as being influential (e.g. 7). The KCL team also introduced micro endoscopy and minimal therapy to China in 2005 by holding practical demonstrations and teaching sessions and arranging for the manufacturers of micro endoscopes to meet up with Chinese surgeons. Since then, a number of publications indicate the adoption of MIT into their health system (e.g. 8).

Improving Devices

Researchers at KCL have worked closely with the German company PolyDiagnost, who produce the micro endoscopes used during MIT, to help guide them in the development of their specialised instruments. The firm attests that this couldn't have been done without the expertise of the KCL team. This is reflected in the company website noting the ENT department at GH/KDI as among their "selection of innovative hospitals with centers for minimally invasive imaging diagnosis and therapy" and in their citing of Karavidas 2010 and Iro 2009 as referenced on their website. They also attest to Prof McGurk's overseas demonstrations of MIT being a major reason for technique dissemination and micro endoscope sales in Europe, India and China (9).

5. Sources to corroborate the impact

1) Clinical Practice
   a. Guy's and Thomas' Hospital Ear, Nose and Throat Specialities: http://www.guysandstthomas.nhs.uk/our-services/ent/specialties/specialties.aspx
   b. King's College Hospital Oral and Maxillofacial Surgery: http://www.kch.nhs.uk/service/a-z/maxillofacial-surgery
   c. King's College London Dental Institute press release: http://www.kcl.ac.uk/dentistry/news/records/2010/feb/salivarystones.aspx
   d. Mail Online article. Published 2.Feb.2010: http://www.dailymail.co.uk/health/article-1247836/They-sound-bizarre-saliva-stones-grow-mouth-ruining-appetite-making-chewing-agony--theyre-far-common-everyday-ailments.html
2) Second International Conference on Controversies in Management of Salivary Gland Disease in Paris in 2008. Programme available on request
3) The London Salivary Gland Centre: http://www.salivary-gland.co.uk/
4) Obstructive Salivary Disease in the European Association of Oral Medicine Handbook: http://www.eaom.eu/empty_24.html
5) Controversies in the Management of Salivary Gland Disease. Second Edition. Eds. McGurk M, Combes J. http://ukcatalogue.oup.com/product/9780199578207.do#.UfZPyo2ce8A
6) Johns Hopkins Medicine Newsletter. Stones in Salivary Glands: A New Look. April 1, 2013: http://www.hopkinsmedicine.org/news/publications/physician_update/physician_update_spring_2013/stones_in_salivary_glands_a_new_look
7) Witt RL, et al. Minimally invasive options for salivary calculi. Laryngoscope 2012;122:1306-11. Doi: 10.1002/lary.23272 (cites Iro H and a number of KCL review papers/book chapters with the above-discussed references)
8) Liu DG, et al. Sialoendoscopy-assisted sialolithectomy for submandibular hilar calculi. J Oral Maxillofac Surg 2013;71(2):295-301. Doi: 10.1016/j.joms.2012.02.016
9) Polydiagnost
   a. Letter supporting GH/KDI's role in development and production of micro endoscopes on file
   b. Website: http://www.polydiagnost.com/english/publikat_ENT_en.html
   c. References: http://www.polydiagnost.com/english/profil-referenzen.html