



PhD Dissertation

**Cone beam computed tomographic  
analysis of vascular structures in the  
maxillary sinus prior to sinus lift  
surgery**

María José Loira Gago

FACULTAD DE MEDICINA Y ODONTOLOGÍA

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Dr. Pablo Ignacio Varela Centelles Profesor Asociado de la Facultad de Medicina y Odontología de la Universidad de Santiago de Compostela,

Dra. Lucia García-Caballero Pérez, Tutora clínica de Patología y Terapéutica Dental y de Odontología en Pacientes Médicamente Comprometidos de la Facultad de Medicina y Odontología de la Universidad de Santiago de Compostela,

HACEN CONSTAR:

Que el trabajo de investigación que presenta Dña. María José Loira Gago titulado “Cone beam computed tomographic analysis of vascular structures in the maxillary sinus prior to sinus lift surgery” ha sido realizado bajo nuestra dirección, supervisando en todo momento su elaboración.

Que nuestro criterio reúne las características de rigor, originalidad y mérito suficientes para optar al grado de Doctor y ser elevado al superior juicio del Tribunal designado a tal efecto.

Para que así conste, a efectos de justificar los mencionados extremos ante los órganos competentes de la Universidad de Santiago de Compostela, abril de 2017.

Fdo. Pablo I. Varela Centelles

Fdo. Lucía García-Caballero Pérez

Fdo. María José Loira Gago  
(doctoranda)



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# 1. INTRODUCTION

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## 1. INTRODUCTION

### 1.1. Maxillary sinus, general concepts.

The paranasal sinuses are four-paired air containing bony spaces present around the nasal cavity, usually lined by respiratory mucous membrane. Their functions are:

- Decrease skull weight.
- Impart resonance to voice.
- Mucus production and storage.
- Humidify facial contour.
- Immune action.
- Conserve heat from nasal fossae.
- Moisturize air.
- Filter debris.
- Dampen pressure differential during inspiration.
- Limit extent of facial injury from trauma.
- Serve as accessory olfactory organ

The maxillary sinus (MS), also known as the antrum of Highmore (1651), are normally located bilaterally in the maxilla. They are the largest of the paranasal cavities, which include the ethmoid, frontal, and sphenoidal sinuses. A pneumatic space, it communicates with the external environment by way of the middle meatus and nasal vestibule. The flow of mucus follows an upward course along the cavity walls towards the natural ostium in the superomedial wall, draining into the ethmoidal infundibulum. This mucus courses along the lateral wall and medially along the roof to reach the ostium. Here, the mucociliary flow from the anterior sinuses converges at the ostiomeatal complex and into the posterior nasopharynx and inferiorly into the Eustachian tube orifice in the middle meatus, posterior to the main ostium (Antunes et al, 2009).

The MS is a horizontal, pyramid-shape cavity within the maxillary bone with a base and four walls: superior, inferior, lateral and anterior.

The base of this pyramid is formed by the lateral nasal wall and the tip within zygomatic buttress. The roof of the MS is also the floor of the orbit and accommodates the infraorbital canal. It communicates with the nasal cavity via the semilunar hiatus, located in the posterosuperior area of the sinus cavity just below the concha nasalis media. Anteriorly, the MS will normally extend from the pyriform aperture to the zygomatic suture, and to the alveolar process inferiorly and the canine or premolar region, although this may vary considerably. The posterolateral wall is made up of the zygomatic bone and the greater wing of the sphenoid bone in the maxillary tuberosity. The sinus floor is formed by the junction of the anterior sinus wall and the lateral nasal wall and it is in a close relationship with the posterior teeth. It usually takes a downward convex route with the deepest point in the first-molar region. (Figure 1).



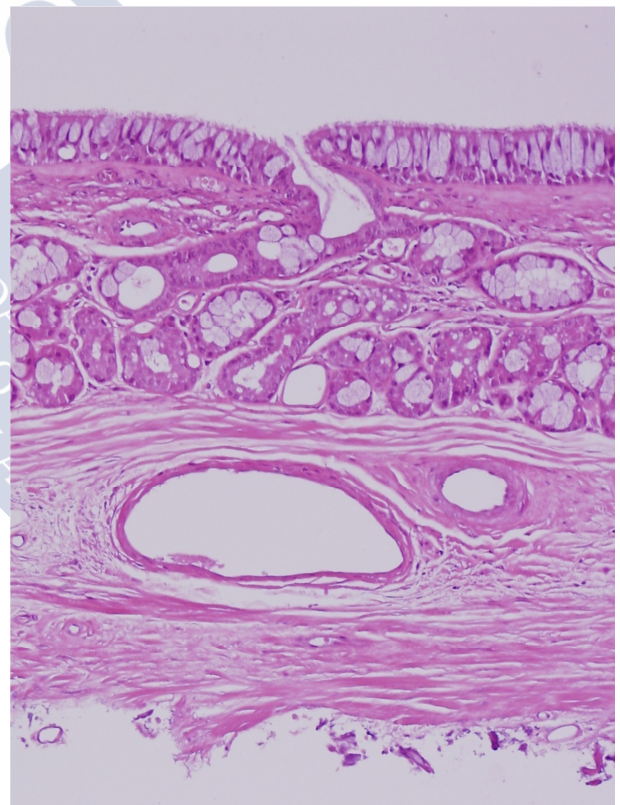
**Figure 1:** Maxillary sinus osteotomy at the anterior sinus wall in a cadaveric dissection.

The MS is the first sinus to develop. It begins to form at 10 weeks of gestation during the process of primary pneumatization, originating in the middle meatus and extending into the ethmoid cartilage. At 20 weeks of gestation, when secondary pneumatization occurs, it extends into the ossifying maxilla. During foetal

development, the MS enlarges to form the nasal cavity (NC) with the maxilla and other surrounding nasal bones.

The MS begins as an evagination of the mucous membrane in the lateral wall of the middle meatus when nasal epithelium invades maxillary mesenchyme (Kitamura, 1989). From the age of 0 till 3-4 years it has an ovoid appearance. The size and width then increase with facial growth. Over 9-12 years the antral floor is at the same level as the nasal floor, assuming a pyramidal shape. On puberty it is 5-12mm below the nasal floor. In old age it starts the reabsorption of the alveolar ridge and thinning of the sinus walls. MS growth is determined by bone restructuring known as pneumatization. During youth, the pneumatization process is proportional to MS growth however with age, pneumatization exceeds MS growth in the sinus floor direction so the alveolar ridge becomes smaller. When the posterior teeth are lost this effect is even more pronounced (Kitamura, 1989).

The mucosal lining of the MS (also known as the Schneiderian membrane) consists of normal ciliated respiratory epithelium covering a thin layer of connective tissue (Figure 2). It ranges in thickness between 0.45 and 1.40mm. A number of factors are commonly associated with increased membrane thickness: thick biotype and history of chronic sinus inflammation. In contrast, smokers tend to have a reduced membrane thickness (Aimetti et al, 2008; Hadar et al, 2009). A thin membrane increases the risk of intraoperative perforation; any intraoperative findings that can help predict membrane thickness are potentially useful when preparing for the surgical procedure.



**Figure 2:** Optical microscopy from the maxillary sinus membrane.

## 1.2. MS vascularization.

The maxillary vascular network is extensive guaranteeing a high amount of blood flow. The haematic contribution to the MS is guaranteed by 3 main arteries, ramifications of the maxillary artery: the Infraorbital Artery (IOA), the Posterior Lateral Nasal Artery (PLNA), and the Posterior Superior Alveolar Artery (PSAA) (Chanavaz, 1900).

In the anterior lateral wall the PSAA divides into 2 branches. An external branch (gingival) is directed toward the superior buccal fornix and maxillary tuberosity, supplying the part of the cheek and the mucosa that covers the alveolar process of the molars and premolars. An internal branch (dental) extends forward and downward, passing under the zygomatic process and then rising in the direction of the orbit, making a true circular anastomosis with the IOA. Such anastomoses guarantee the haematic contribution to the sinus membrane, to the periosteal tissues, and specially, to the anterior lateral wall of the sinus (Hur et al, 2009; Rosano et al, 2009). The Alveolar Antral Artery (AAA) is an anastomosis of the PSAA and the IOA.

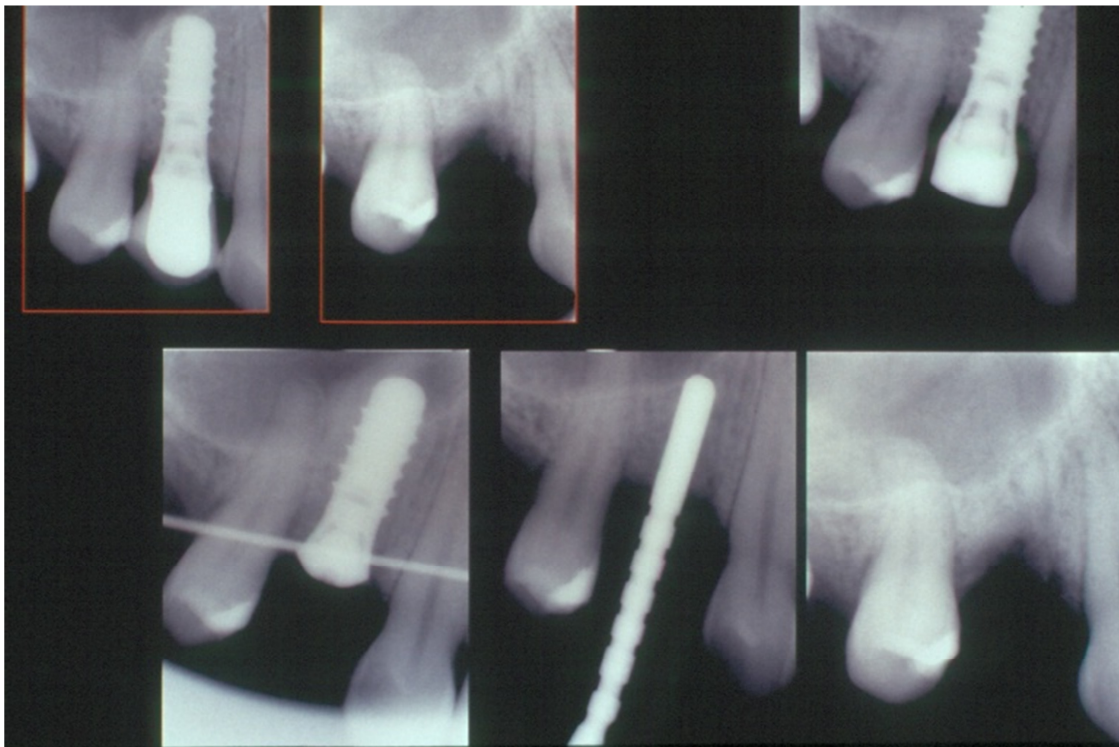
Before leaving the infraorbital canal through the infraorbital foramen, some branches of the IOA course either medially, thus participating in the vascularization of the medial sinus wall, or in the lateral direction by anastomosing with the AAA in the anterior portion of the MS (Solar et al, 1998).

The medial or nasal wall of the MS is vascularized also by the posterior lateral nasal arteries that, after supplying the superior and medial conchae, pass through the wall in an anteroposterior direction to irrigate the sinus mucosa.

In the posterior wall of the MS the PSAA runs close to the periosteum of the maxillary tuberosity, with several branches spreading out over the whole posterior sinus wall and contributing to this vascularization. There is a close anatomic relationship between the sinus posterior wall, the descending palatine artery, and the sphenopalatine artery (Rosano, 2009).

### 1.3. Rehabilitation with implants in the subsinusal area.

Missing teeth may result in a functional and cosmetic deficit and have traditionally been replaced with dentures or bridges. Dental implants offer an alternative; they are inserted into the jawbones and used to support dental prostheses (Figure 3), (Esposito, 2010).



**Figure 3:** Images from intraoral radiology during implant placement with transcrestal technique above the maxillary sinus.

Dental implants rely on the maintenance of a direct structural and functional connection between living bone and the implant surface. This is termed osteointegration and was first described by Brånemark,(1983).

Insufficient bone volume is a common problem encountered in the rehabilitation of the edentulous posterior maxilla with implant-supported prostheses. The bone available for implant placement may be limited by the presence of the MS together with loss of alveolar bone height (Garg, 1999).

After tooth loss, atrophy of the alveolar crest is a typical occurrence. This is due to the absence of chewing forces in the jaw and can lead to a complete loss of the alveolar crest in edentulous patients (Gaheitner, 2003).

Cawood and Howell (1991) have described and classified the bone volume loss in anatomical randomized clinical trials, which measured the changes observed on edentulous jaws. This classification identifies six types of residual ridges:

- Class I: dentate.
- Class II: immediately post extraction.
- Class III: well-rounded ridge form, adequate in height and width.
- Class IV: Knife-edge ridge form, adequate in height and inadequate in width.
- Class V: Flat ridge form, inadequate in height and width.
- Class VI: Depressed ridge form, with some basilar loss evident.

Resorption takes place in an apical direction and occurs together with an increase in sinus pneumatization as a consequence of intrasinus positive pressure. As a result, the sinus floor is closer to the alveolar ridge (Cawood & Howell, 1991).

The MS, will normally extend anteriorly from the second molar to the canine or premolar region, although this varies considerably. The sinus floor will usually take a downward, convex route with the deepest point in the first-molar region. As was previously mentioned, pneumatization is seen throughout adolescence, and secondary pneumatization may follow the loss of posterior maxillary teeth reducing significantly the residual ridge volume (Katsuyama & Jensen, 2001). Following tooth extraction or loss, an initial buccopalatal reduction of bone volume occurs due to the interrupted blood supply to the bone plate and to the absence of occlusal loads. Conical elevations projecting into the cavity, reflecting the roots of the maxillary molars and premolars, are frequently observed. Bony walls or septa may project into the cavity from the sinus floor and lateral wall (Katsuyama & Jensen, 2001). The reduced vertical bone height in the posterior maxillary region often limits standard implant placement.

The rehabilitation of edentulous patients with dental implants has become a highly predictable treatment (Albrektsson, 1986; Adell, 1990) and good bone quality and

quantity are required. Posterior areas of the maxilla can be a therapeutic challenge due to the anatomical limitations and the poor bone quality (Atwood, 1971).

To solve this problem several alternatives have been suggested: the placement of an onlay bone graft over the edentulous alveolar ridge for horizontal or vertical bone augmentation (Esposito, 2009). Implants can also be placed with angulation in order to avoid the MS when anatomical conditions permit (Esposito, 2009). Zygomatic implants offer an alternative as they are long implants which pass through the sinus or laterally from the sinus into the zygomatic process (Esposito et al, 2005). Sinus lift procedures utilise short implants offering the option of a less complex, cheaper and faster alternative to augmentation (Srinivasan et al, 2013).

### **1.4. Introduction to SLS: different surgical techniques.**

The most commonly used technique to increase the bone height before placing dental implants is sinus lift surgery (SLS). This surgical procedure aims to create increased bone volume in the MS floor in order to enable installation of implants in the region. The graft in the sinus bottom may be left to heal primarily before implants are placed in a second surgery (2 stage procedure), or implants may be placed simultaneously with the graft (1 stage procedure) (Johansson et al, 2001).

The first SLS was done by Oscar Hilt Tatum, Jr in February 1975. After his intervention in the “Alabama Implant Congress” he placed two dental implants together with a prosthetic rehabilitation.

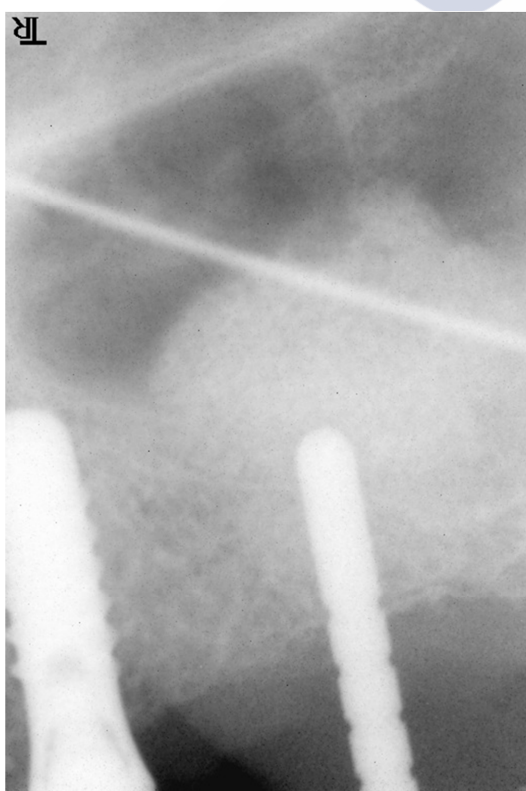
Dr Philip Boyne was introduced to this technique by Dr Tatum in the annual meeting of The American Academy of Implant Dentistry 1977.

Boyne & James in 1980 described a two-stage procedure, where the MS was grafted using autogenous particulate iliac bone at the first stage of surgery. After approximately 3 months, a second stage surgery was performed to place the implants, later used to support fixed or removable reconstructions.

The evolution of this technique was reported each year until 1986 when an article was published describing the procedure (Tatum, 1986).

The basic surgical principle and technique have not significantly changed ever since. Intraoral access to the MS is gained through the oral mucosa in the oral region of the anterior MS wall. A bony window is prepared, and the sinus membrane is dissected and lifted from the sinus floor in order to enable insertion of a graft alone, or around installed implants to facilitate bone formation in the created secluded space. The SLS has developed over time, and several minor variations now exist (Ribben & Thor, 2012). The wishes of patients and dentists for minimally invasive methods have led to the development of new techniques (Abadzhiey, 2009).

Seeking a less invasive method, in 1994 Summers made the surgical protocol, offering crestal access with the aim of reducing membrane perforations with the lateral approach gaining 3-5mm of bone high in a safer way (Mongalo, 2012).



A crestal incision is followed by a small osteotomy through the alveolar crest of the edentulous ridge at the inferior border of the MS. This intrusion osteotomy procedure elevates the sinus membrane, thus creating a tent-like space. This provides space for bone graft placement or blood clot formation. Different diameter sizes are used to expand the maxillary bone until the ideal diameter to place the implant is reached without using drills, just using osteotomes (Figure 4).

**Figure 4:** Sinus lift surgery with crestal approach using osteotomes

Grafting material is added incrementally to the osteotomy site and condensed until the desired bone height is reached (Summers, 1994).

It should be noted that the bone grafts are placed blindly into the space below the sinus membrane so it is possible to perforate the Schneiderian membrane. Later Summers's technique was modified and the original concave cutting osteotomes were replaced by convex and rounded ones for safely compression of bone after preparing the pilot hole. If a perforation occurs, it is still possible to change to a lateral window technique SLS (Jensen & Terheyden, 2009).

This SLS technique has some advantages over the conventional lateral-window procedures. It is a less invasive surgery with a smaller flap design and a less extensive osteotomy. Therefore, there is less chance of postoperative complications and morbidity, and patient acceptance for surgery is greatly increased. Also the amount of graft material is less than the needed with the lateral approach.

This technique may be beneficial especially in a situation where the patient has a clear contraindication to conventional approach because of space occupying masses such polyps, retention cysts, or mucosal thickening (Tat Chang et al, 2008).

One of the limitations of this technique is the requirement of at least 6mm of residual bone to ensure primary stability. Patients with more atrophic crest will have to be approached through the lateral wall technique (Mongalo, 2012). Another restriction is the limited amount of bone height to be gained (1-2mm) (Abadzhiev, 2009).

Another technique with crestal access is the balloon sinus lift first described by Munoroi (2003). Some years later Kfir et al (2006) described the crestal access with the balloon technique known as MIAMBRE (Minimally invasive antral membrane balloon elevation) placing the implants and the graft in the same intervention.

The osteotomy was enlarged by an osteotome of 2.8mm to 3.15mm, and the sinus floor was gently broken. After examining the integrity of the sinus membrane (by

Valsalva manoeuvre and direct visualization), Fisiograft gel (GHIMAS<sup>®</sup>, Casalecchio di Reno, Italy) was injected to enhance lubrication (Kfir et al, 2006).

A sleeve (2.6mm internal diameter) was screwed in up to 0.5mm superior to the sinus floor. A dedicated inflatable balloon (inflated volume  $\leq$  2.5 ml) was advanced 1mm to 2mm beyond the tip of the metal sleeve and anchored by a locking mechanism at the proximal part of the sleeve. The balloon was slowly inflated with the dedicated inflator syringe using diluted contrast media (50% Ultravist 370 diluted with normal saline), with inflating pressure not exceeding 2 atmospheres (Kfir et al, 2006). In this way the Schneiderian membrane is raised leaving space for the grafting material.

Aside from its higher cost, this technique is accessible with predictable results. An additional advantage is that we know in advance the free space volume and the graft volume need. It can also be done on residual crest of 3mm or less, while the osteotomes technique requires at least 6mm (Kfir et al, 2009).

Recently, in 2013, Ziv Mazor et al described a simplified minimally invasive transalveolar sinus elevation technique utilizing calcium phosphosilicate (CPS) putty for hydraulic sinus membrane elevation. This technique is based on the application of hydraulic pressure via a viscous bone graft that acts as an incompressible fluid, which helps Schneiderian membrane elevation (Ziv Mazor et al, 2013).

### **1.5. When is a SLS required and which techniques and materials are the most appropriate?**

There are numerous articles in the literature, assessing the survival rates of grafts and implants placed with a SLS and testing whether and when augmentation of the MS is necessary.

For example, in 2003 Wallace et al published a systematic review about the effect of sinus augmentation on the survival of endosseous dental implants. In this report, the survival rate of implants placed in sinuses augmented with the lateral window technique varied between 61.7% and 100%, with an average survival rate of

91.8%. Implant survival rates reported in this systematic review compared favourably to reported survival rates for implants placed in the non-grafted posterior maxilla. Rough-surfaced implants have a higher survival rate than machine-surfaced implants when placed in grafted sinuses. Implants placed in sinuses augmented with particulate grafts show a higher survival rate than those placed in sinuses augmented with block grafts. Implant survival rates were higher when a membrane was placed over the lateral window. The utilization of grafts consisting of 100% autogenous bone or the inclusion of autogenous bone as a component of a composite graft did not affect implant survival. There was no statistical difference between the covariates of simultaneous versus delayed implant placement, types of rough-surfaced implants, length of follow-up, year of publication, and the evidence level of the study.

It was concluded that the data was insufficient to statistically evaluate the effects of smoking, residual crestal bone height, screw versus press-fit implant design, or the effect of implant surface micromorphology other than machined versus rough surfaces. There were also insufficient data to recommend the use of platelet-rich plasma in SLS (Wallace et al, 2003).

Pjetursson et al published another systematic review in 2008 to assess the survival rates of grafts and implants placed in sites with sinus augmentation via lateral approach, with a mean residual bone height of 6mm or less, and to evaluate the incidence of surgical complications. The implant survival into 3 years, based on implant level, was 90.1% (95% CI: 86.4%-92.8%). Based on subject level the estimated annual failure was 6.04% (95% CI: 3.87%-9.43%) translating into 16.6% (95% CI: 10.9%-24.6%) of the subjects experiencing implant loss over 3 years. The annual failure rate of machined surface implants (6.9%) was significantly ( $p < 0.001$ ) higher than that for rough surface implants. The 3 years survival rates of rough surface implants ranged between 96.3% and 99.8% depending on the grafting material. The lowest failure rate (0.1%) of rough surface implants was observed using autogenous particulated bone graft. The annual failure was also significantly higher (4.0% vs 0.7%) when no membrane was used. The most frequent complication was sinus membrane perforation (19.5%). Graft loss resulting in impossibility of implant placement was reported in 1.9% of cases and graft infection in 2.9%.

This systematic review revealed several shortcomings in the clinical studies reporting on SLS. Many of the studies on the survival of implants placed in sinus grafted sites failed to report both on the residual bone height at the site of presumptive implant placement and on graft failures. There is also a lack of randomised controlled trials (RCTs) with sufficient statistical power comparing various grafting materials (Pjetursson et al, 2008).

In 2010, Esposito et al published another systematic review to test the null hypothesis that there is no difference in the success, function, complications and patient satisfaction with and without augmentation and between different SLS techniques for dental implants. This included looking at whether a SLS procedure is necessary and which is the most effective augmentation technique.

Their conclusions were based on few trials with few patients, sometimes with a short follow-up and often being judged to be at high risk of bias. One trial investigation concluded that it is still unclear when SLS procedures are needed. Implants of 5 and 6mm long can be successfully loaded in maxillary bone with a residual height of 4-6mm below the sinus without any augmentation procedure.

In the other nine trials investigated it was concluded that if the residual alveolar bone height is 3 to 6mm, a crestal approach to lift the sinus lining and place 8mm implants may lead to fewer complications than a lateral window approach placing 10mm implants. Keeping the sinus lining elevated with a rigid resorbable barrier in the presence of 1 to 5mm of residual bone without the addition of a graft is sufficient to regenerate new bone. They also concluded that Bio-Oss<sup>®</sup> and Cerasorb<sup>®</sup> might be as effective as autogenous bone grafts, and platelet-rich plasma (PRP) may not improve the outcome of SLS procedures for implant rehabilitation (Esposito et al, 2010).

No RCTs have been performed to compare the simultaneous and staged SLS approaches in identical clinical situations. A review of the literature has, however, suggested that both approaches may involve similar rates of implants survival (Del Fabro et al, 2008).

Simultaneous SLS refers to elevation of the sinus floor during the same session as implant placement. In the past, a generally held rule was that simultaneous SLS was appropriate at sites offering a residual bone height of 5mm. Primary stability is, however, influenced by bone density and loosely structured trabecular bone. Staged SLS is recommended whenever adequate primary stability cannot be obtained. A waiting period of 3 to 4 months may be appropriate in single-tooth gaps if the sinus anatomy is narrow and an autograft (alone or in combination with a bone substitute) is used for augmentation. A total of 10 to 12 months are required for graft consolidation before implants can be predictably inserted in an “eggshell” sinus floor when augmented with a bone substitute alone (Katsuyama & Jensen, 2011).

Further research to evaluate in which clinical situations a SLS is positive for patients and to know which are the most effective surgical procedures would be desirable.

### **1.6. Lateral window technique for maxillary sinus augmentation.**

SLS with lateral window technique is the most commonly used approach because it offers good long-term results using different kinds of bone grafts and implants (Galindo-Moreno et al, 2007).

There is strong evidence for the lateral window technique as a predictable procedure for SLS using a simultaneous or staged approach (Jensen & Terheyden, 2009).

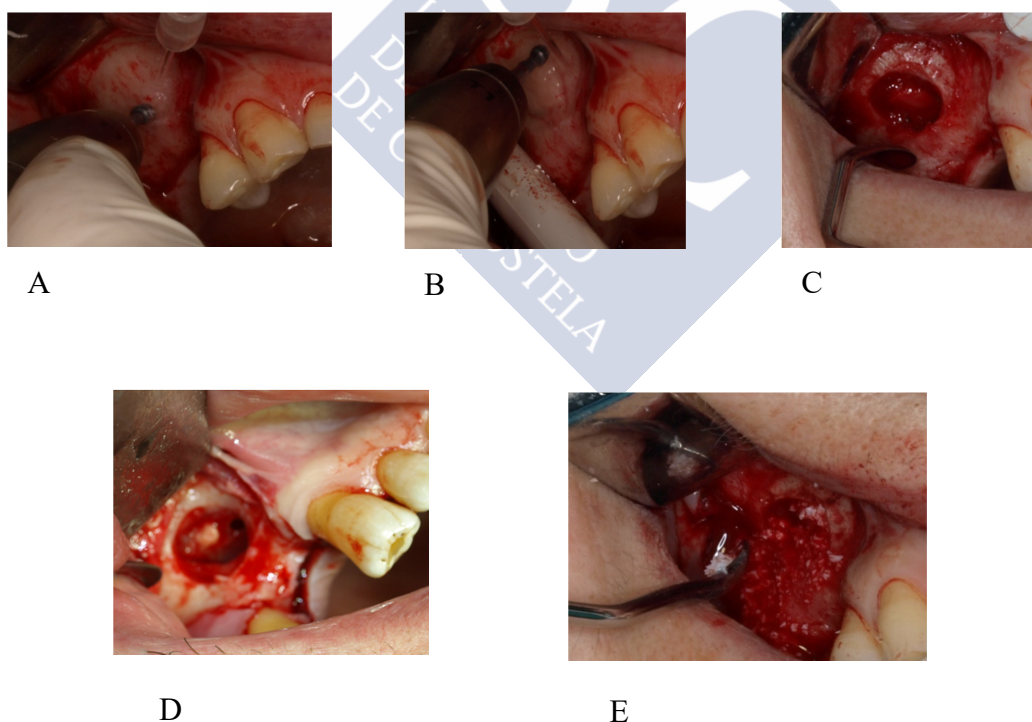
With the lateral window technique it is possible to obtain greater bone volume. According to Pjetursson et al, with a crestal approach is possible to gain 2-3mm more height but if a 10mm implant is preferred and the residual ridge is less than 7mm, then this technique is of limited use (Pjetursson et al, 2009).

A systematic review in 2008 concluded that the implant survival after a SLS with a transcrestal approach is dramatically reduced if the initial residual bone is 5mm or less (Tan et al, 2008).

Lateral window SLS requires a crestal incision followed by a mucoperiosteal flap and a complete soft tissue debridement.

The window size and position are determined in accordance with anatomic conditions. While rotary instruments are commonly used for window preparation, the recent development of piezoelectric ultrasonic devices may contribute to reducing intraoperative complications such as membrane perforation (Wallace et al, 2007).

Osteotomy should follow the outline of the sinus and should not be more than 3mm away from the floor. The corners of the access window are usually rounded as sharp corners may increase the risk of membrane perforation when a trap-door approach is used. The window should be large enough to allow access for instrumentation. Curettes are used to carefully elevate the sinus membrane and should always be maintained on the bony walls to avoid membrane perforation. The sequence of membrane elevation is from the sinus floor, towards the posterior wall, superior wall and finally the anterior wall (Figure 5) (Battal & Norris, 2013).



**Figure 5:** Surgical sequence for SLS with lateral approach: A. Starting the osteotomy. B. Finishing the osteotomy. C. Visualization of Schneiderian membrane after removing bone fragment. D. Elevation of the Schneiderian membrane. E. Bone grafting material introduction in the MS.

It is recommended to do the Valsalva manoeuvre to check for the integrity of the Schneiderian membrane. The space created after sinus membrane elevation is grafted with optional materials such as: xenografts, allografts or alloplastic materials. A collagen resorbable membrane is used to cover the window and the mucoperiosteal flap is then repositioned and sutured (Battal & Norris, 2013).

### **1.7. Contraindications and complications of MS augmentation.**

As stated at the 1996 Consensus Conference at Babson College, a SLS is a safe and predictable procedure for increasing alveolar bone height in the postero-superior alveolar regions of the maxilla in order to allow oral rehabilitation and restore masticatory function, however it is not free from complications.

SLS is contraindicated in patients who have been irradiated, received full dose radiotherapy or take IV bisphosphonates. High-risk factors include poorly controlled acute sinusitis and chronic periodontitis. Smoking combined with a history of periodontitis is a risk factor for implant survival and biological complications in general (Heitz-Mayfield & Hyunh-Ba, 2009). Abnormalities of the sinus membrane such as hypertrophy are not a contraindication but should be considered as a relative risk (Katsuyama & Jensen, 2009).

During the surgical procedure the risk of complications must be considered and the appropriate treatment provided. The most frequently encountered complication was the perforation of the sinus membrane which occurred in 19.5% of the interventions according to Pjetursson (Pjetursson et al, 2008) but this can vary from 0% (Galindo-Moreno et al, 2007) to 58.3% (Krennmair et al, 1997).

Accidental bleeding secondary to surgical damage of AAA is the second most common complication of SLS (Maridati et al, 2014). Observational studies and case series highlight the fact that up to 20% of major bleeding events during SLS surgery are due to AAA damage (Elian et al, 2005; Flanagan et al, 2005). This damage may indirectly result in postponement of the surgery, a slower surgical procedure, reduction

of blood supply, mobilisation of the graft, and also in an increase in the frequency of membrane perforations (Maridati et al, 2014).

The AAA is an anastomosis of the PSAA and the IOA, which has been repeatedly identified by dissection in 100% of the lateral sinus walls of cadavers (Solar et al, 1999; Hur et al, 2009; Rosano et al, 2009; Sato et al, 2010; Kqiku et al, 2013). AAA can follow either a straight or a U-shaped course in the anterolateral wall of the sinus, whose closest point to the alveolar crest is at the site of the first or second molar (Mardinger et al, 2007; Jung et al, 2011). Its relationship with the bony wall is also variable, being most commonly completely intraosseous and rarely (less than 8%) superficial, on the outer cortex under the periosteum of the sinus lateral wall (Jung et al, 2011; Ilgüy et al, 2013). In patients with an artery with a diameter higher than 0.5mm (between 1-2mm) the risk of haemorrhage is 57%, and in these patients the probability of symmetric distribution of the artery is 70% (Zijderveld et al, 2008).

The damage of a small vessel (< 1mm) has a low impact on the surgical procedure (Mardinger et al, 2007), but wider diameters may compromise visualization and make surgery more difficult (Zijderveld et al, 2008). The detection of arteries with more than 3mm can prevent important iatrogenia (Testori et al, 2010; Rosano et al, 2011).

Flanagan (2005) states that bleeding can be controlled with: head elevation to decrease nasal blood flow, tamponade, an intranasal balloon catheter, ice, electrocautery, diathermy or percutaneous arterial embolization. Endoscopic ligation by an appropriately trained surgeon may also be indicated. Ella et al (2008) recommend using a gauze to control bleeding and avoiding electrocautery due to the high risk of Schenederian membrane perforation. This approach is also suggested by Cameron (2010) when facing a prolonged pulsatile haemorrhage. Sponges saturated with topical thrombin are also indicated because of their direct effect over the coagulation cascade to form a haemostatic clot at the site of the bleeding vessel.

Bleeding may condition the surgical approach, making careful surgical planning mandatory, paying special attention to a correct identification of the AAA to avoid undesired complications (Zijderveld et al, 2008).

Although anatomical studies found an intraosseous anastomosis between the dental branch of the AAA and the IOA in 100 % of the cases, the CT may not identify these structures in some patients (Elian et al, 2005). However, and since Verdadi (2006), revision reporting an increasing detection accuracy of CT and CBCT for AAA detection in the lateral wall of the MS, a series of reports have been published (Anamali et al, 2013).





## 2. JUSTIFICATION AND OBJECTIVES

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## 2. JUSTIFICATION AND OBJECTIVES

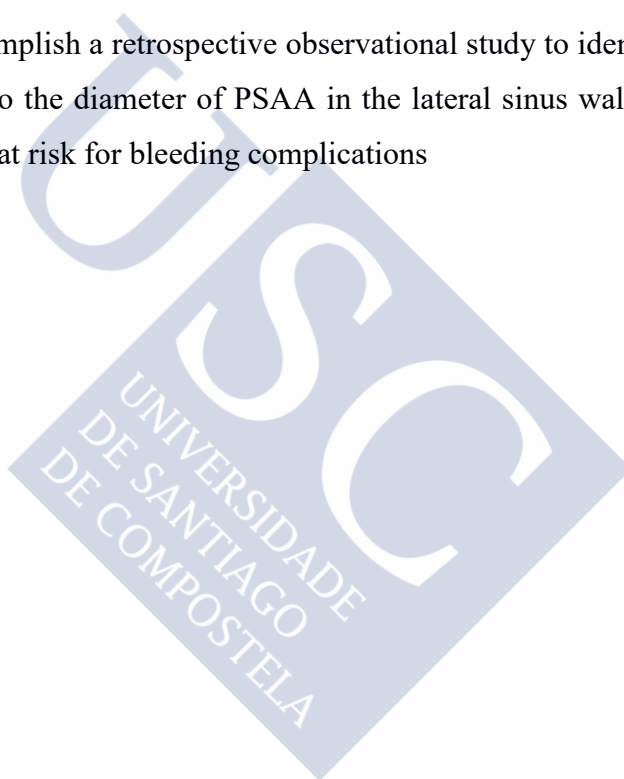
Perforation of the sinus membrane is the most frequently reported intraoperative complication of SLS procedures, reported in up to 19.5% (0-58.3%) of the cases (Pjetursson et al, 2008). The second most common complication is severe bleeding, mostly during antrostomy while using rotatory instruments (Kang et al, 2013). As accidental blood vessel damage may cause massive bleeding (Chang & Wang, 2011), careful surgical planning is paramount (Flanagan, 2005; Chan & Wand, 2011) particularly because the intra-osseous anastomosis between the PSAA and the IOA have been linked to potential haemorrhagic complications (Elian et al, 2005; Rosano et al, 2009).

Accidental damage of these vessels is reported to account for up to 20% of major bleeding events (Elian et al, 2005; Flanagan, 2005), although some case series have described lower incidences (Zinderveld et al, 2008). As severe postoperative haemorrhages have also been described following transcrestal SLS procedures (Jensen et al, 2012), accurate identification of vascular structures prior to surgery is mandatory to avoid undesired complications (Ziderverld et al, 2008).

Anatomical studies have consistently detected intraosseous PSAA anastomosis in every MS (Solar et al, 1999; Hur et al, 2009; Rosano, 2009) but CT scans failed to identify these structures in many patients (Elian et al, 2005) and consequently its use for this purpose has been discouraged (Verardi, 2006). Nevertheless, multiple imaging studies have been developed since publication of this evidence-review article (Verardi, 2006) increasing the capability of CT and CBCT for detecting PSAA within the sinus wall (Anamali et al, 2013). These circumstances would seem to justify proposing these main objectives for this investigation:

1. Carry out a Systematic Review and meta-analysis to assess the prevalence of the PSAA in the lateral sinus wall using CT/CBCT in patient candidates for SLS.

2. Gather further information on the prevalence of the PSAA detection by CBCT and to study the variables related to its detection while allowing for potential confounding factors.
3. Perform a retrospective observational study to identify and model the variables related to patients at risk of iatrogenic bleeding during SLS whose PSAA are located within 15mm of the bony crest and explain the PSAA course variations at the anterolateral sinus wall extending beyond the safe-distance.
4. To accomplish a retrospective observational study to identify variables related to the diameter of PSAA in the lateral sinus wall and identify profiles at risk for bleeding complications



# 3. REPORT OF RESEARCH

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### 3. REPORT OF RESEARCH

In order to address the aim of this research, the analysis will be carried out from four perspectives, all independently presented, whose methodology will also be specifically explained.

#### **3.1. CHAPTER I: Detection of the posterior superior alveolar artery in the lateral sinus wall using computerised tomography/cone beam computerised tomography: A prevalence meta-analysis**

##### **3.1.1. Abstract**

**Objective:** To assess the prevalence of the PSAA in the lateral sinus wall using CT/CBCT in candidates for sinus lift.

**Materials and methods:** A systematic search of MEDLINE, Embase, and Proceedings Web of Science databases was carried out. Studies were included if they provided data on PSAA detection at the bony wall using CT and/or CBCT, and the report included subsinus edentulism. Exclusion criteria were as follows: report on post-mortem findings, mixed samples (living and cadaveric), presented pooled results only, studies performed for suspected sinus pathology. Heterogeneity was checked using an adapted version of the DerSimonian and Laird Q test, and quantified by calculating the proportion of the total variance due to between-study variance (I<sup>2</sup> statistic).

**Results:** The search identified 811 single papers that were reviewed and filtered according to the inclusion/exclusion criteria. Ten studies were selected which included 1,647 patients and 2,740 maxillary sinuses (study unit). These reports showed a pooled prevalence of PSAA at the lateral wall of 62.02 (46.33-77.71). CBCT studies revealed

higher frequencies of PSAA detection 78.1 (95% CI=61.2-94.9) when compared to CT studies 51.19 (42.33-60.05). Conventional CT revealed an average thickness of the artery higher than described by CBCT examinations

**Conclusions:** The prevalence of PSAA detection in the sinus lateral bony wall is higher with CBCT in comparison to conventional CT. Still, additional comparative studies that control potential confounding factors are needed to ascertain the actual diagnostic value of radiographic explorations for assessing the PSAA prior to SLS procedures.

**Key words:** Maxillary sinus, artery, posterior superior alveolar artery, sinus floor elevation, meta-analysis.

### 3.1.2. Introduction

Perforation of the sinus membrane is the most frequently reported intraoperative complication of SLS procedures, arising in up to 19.5% (0-58.3%) of cases (Pjetursson et al, 2008). The second most common undesired event is severe bleeding, most commonly occurring when performing the antrostomy using rotary instruments (Kang et al, 2013). Accidental blood vessel damage may cause massive bleeding (Chan & Wang, 2011), therefore careful surgical planning is paramount (Chan & Wang 2011; Flanagan 2005), particularly as the intra-osseous anastomosis between the PSAA and the IOA have been linked to potential haemorrhagic complications (Elian et al 2005; Rosano et al, 2009). The intra-osseous branch of the PSAA within the lateral sinus wall usually describes a straight or U-shaped course (Hur et al, 2009), forming a concave arch whose closest point to the osseous crest is located near to the first molar (Mardinguer et al, 2007; Jung et al, 2011). This anastomosis supplies the Schneiderian membrane, periostium, and the antero-lateral sinus wall (Rosano et al, 2009; Hur et al, 2009; Mardinguer et al, 2007; Jung et al, 2011; Anamali et al, 2013), while contributing to graft integration and healing of the surgical wound (Solar et al, 1999).

Accidental damage of these vessels has been reported to account for up to 20% of major bleeding events (Elian et al, 2005; Flanagan, 2005), although some case series have described lower incidences (Zijderveld et al, 2008). Experimental SLS studies in

edentulous cadaveric material have reported that intraosseous arteries are involved in up to 83% of the cases when antrostomy is performed at the first and second molar level (Rodella et al, 2010). As severe postoperative haemorrhages have also been described following transcrestal SLS procedures (Jensen et al, 2012).

An accurate identification of vascular structures prior to surgery is mandatory to avoid undesired complications (Zijderveld et al, 2008).

Anatomical studies have consistently detected the intraosseous PSAA anastomosis in every MS (Rosano, 2009; Hur et al, 2009; Solar et al, 1999) but CT scans have failed to identify these structures in many patients (Elian et al, 2005) and their use for this purpose has been discouraged (Verardi, 2006). Nevertheless, multiple imaging studies have been developed since this evidence-review article (Verardi, 2006) was published, increasing the capability of CT and CBCT for detecting PSAA within the sinus wall (Anamali et al, 2013). These circumstances seem to justify the need for a systematic review and meta-analysis aimed at assessing the prevalence of PSAA in the lateral sinus wall of SLS patients using CT/CBCT.

### **3.1.3. Methods and materials**

Both methods of analysis and the inclusion criteria were detailed in the study protocol to ensure homogeneous criteria amongst all researchers during the study. The aforementioned protocol was initially conceived for radiological identification of the PSAA within the bony sinus wall.

A systematic search was undertaken in July 2014 of MEDLINE, Embase and Proceedings Web of Science databases (Conference Proceedings Citation Index-Science (CPCI-S)), using the following strategy: ((“blood supply” OR “maxillary artery” OR “arterial supply” OR “vascular”) AND (“maxillary sinus” OR “sinus floor elevation” OR “sinus lift” OR “sinus augmentation”)), both in medical subject headings (MeSH) and in free text words. This search strategy was independently reviewed, discussed by all authors, and supplemented with an additional hand search (Moher et al, 2009) performed at our institution’s library catalogue, considering both books and relevant journals (Figure 6).

Studies were considered if they fulfilled the following eligibility criteria:

- i. To provide data on PSAA anastomosis detection within the sinus lateral bony wall using CT and/or CBCT.
- ii. To report on samples of patients with subsinusal edentulism.

No language restrictions were applied. Studies were excluded either if reported on post-mortem findings, or used mixed samples (living and cadaveric specimens) presenting pooled results only, or on radiographic studies performed for suspected sinus pathology.

Data was retrieved by two investigators (ML & JS) in a standardised manner using a custom-made extraction sheet. Disagreements were resolved by consensus.

### **Quality assessment**

Quality was evaluated by means of a five-item binary scale (yes/no) specifically designed for this study and based upon the STROBE guidelines for reporting observational studies (Von et al, 2007; Hoy et al, 2012):

- i. Does the report give details about study participants? Is there adequate demographic information about the sample (one point).
- ii. Are the aim and the outcome of the study clearly defined? Is the aim of the study is clearly stated and the number of outcome events is detailed (one point).
- iii. Was the sampling group a true or close representation of the target population? Were the radiographic examinations were undertaken for SLS purposes (one point).
- iv. Was the measuring instrument adequately described? Are the equipment, software and measuring instruments are clearly stated (one point).
- v. Does the report give a cautious overall interpretation of the results? Are both the surgical implications and existing evidence discussed (one point).

When information on a specific item was not provided by the authors, we graded the item as “no”. The quality score was independently graded by two investigators (JS & BT).

#### **3.1.4. Data analysis**

The prevalence of the PSAA in the lateral wall of the MS for each study was computed by dividing the number of sinuses in which the artery was detected by the total number of sinuses examined. To determine the 95% confidence intervals (95% CI), we used the exact method proposed by Newcombe and Altman in 2000. We then weighted the study-specific prevalence estimates by the inverse of their variance to compute a pooled prevalence and its 95% confidence interval. We calculated both fixed-effects and random-effects pooled estimates. When heterogeneity is detected, the random-effects model will give more reliable results than the fixed-effects model, including a more conservative (wider) CI. To check for heterogeneity, we used an adapted version of the small samples of the DerSimonian and Laird Q test; and to quantify this heterogeneity we calculated the proportion of the total variance due to between-study variance (Ri statistic), (Takkouche et al, 1999). In our meta-analysis, due to the presence of a considerable amount of heterogeneity between studies, the fixed effects pooled prevalence figures were considerably overestimated and their 95% confidence intervals artificially narrow. Although for the sake of exhaustivity we present both kinds of estimates, we used the random effects estimates as the most adequate figure. All analyses were performed with the software HEpiMA<sup>®</sup> version 2.1.3 (Costa-Bouzas et al 2008).

#### **3.1.5. Results**

The aforementioned search strategy identified 811 single papers. Each abstract was reviewed for contents relevant to the topic of this meta-analysis and 790 were consequently discarded. Finally, 21 papers were filtered for further analysis according to the eligibility criteria set out in this study (Figure 6).

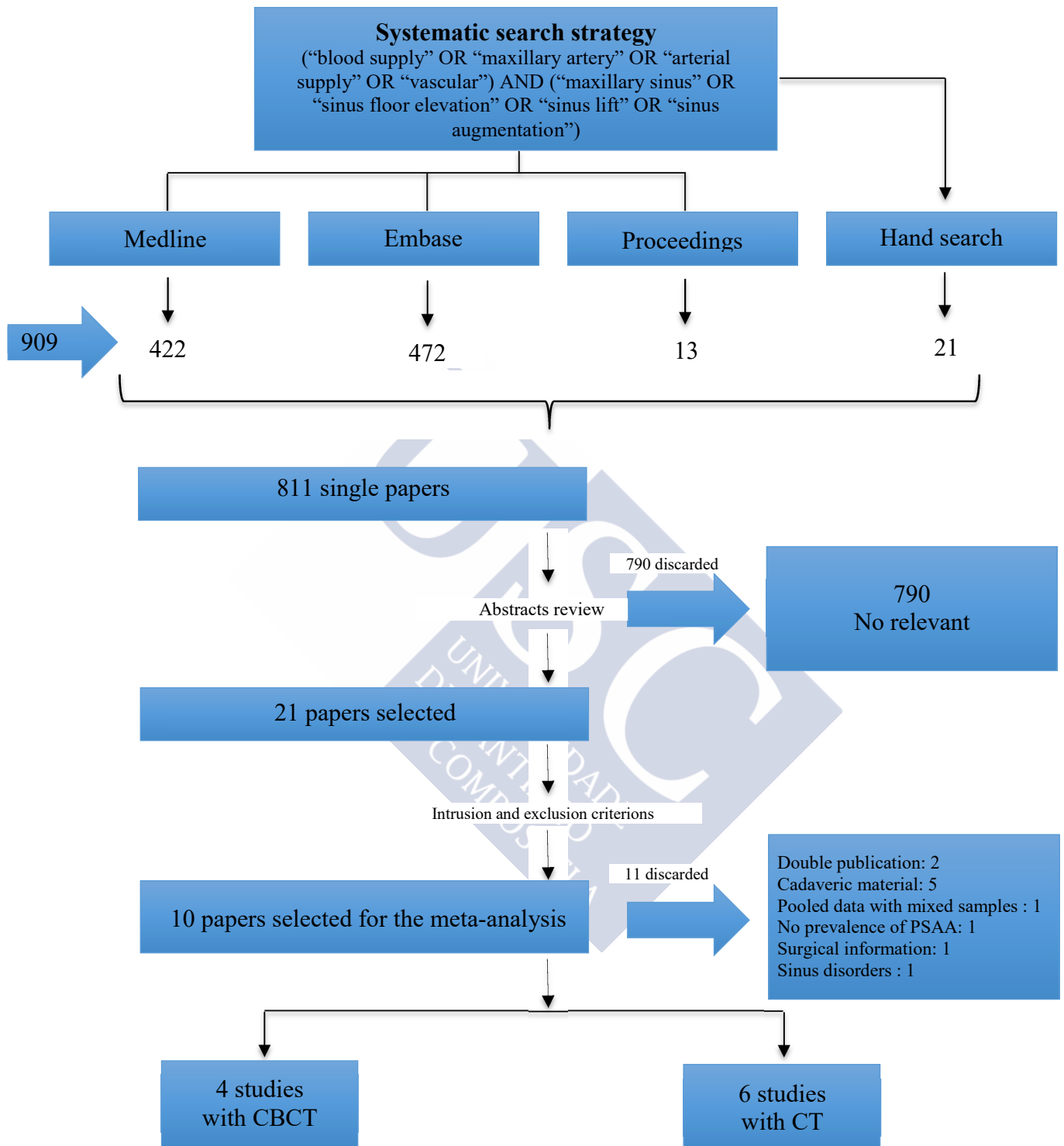


Figure 6. Study flow chart.

Eleven reports did not meet the inclusion criterion of considering samples for patients with subsinus edentulism: one paper provided pooled data from patients and cadaveric material (Ella et al, 2008). Four papers presented data obtained from the same series of cadaveric material: Solar et al (1999) and Traxler et al (1999); and by Yoshida et al (2010) and Sato et al (2010). Another study, aimed to identify the branches of the maxillary artery, but did not provide information on the prevalence within the sinus lateral bony wall (Kwak et al, 2010). One further report was discarded due to its reporting surgical information from a series of cadaveric material (Rodella et al, 2010), and five articles describing prevalence of 100% of PSAA within the sinus wall, based on anatomic dissections, were also excluded from this meta-analysis (Rosano, 2009; Hur et al, 2009; Solar, 1999; Sato et al, 2010; Kqiku et al 2013) (Table 1). Finally, another paper was discarded because CT scans were performed to investigate sinus disorders (Kim et al, 2011).

**Table 1.** Prevalence of PSAA at the lateral sinus bony wall, identified by dissection of cadaveric material

Author, year	Country	N (M/F)	Age X±SD (Mn-Mx)	Maxillary Sinus (n)	Prevalence (%)	PSAA Diameter* (X±SD)	Distance PSSA-alveolar crest (X±SD)	Subsinusal dental pattern
Solar et al <sup>11</sup>	Austria	18 (10/8)	67 (55-75)	18	100	1.6±0.2	19.5±3.6	Edentulous
Hur et al <sup>7</sup>	Korea	42 (18/24)	70 (47-94)	42	100	0.8±0.3	NG	Dentated
Rosano G, <sup>6</sup>	France	15 (-)	76 (59-90)	30	100	NG	NG	NG
Sato <sup>5</sup>	Japon	19 (-)	77.7±9.8 (59-94)	34	100	NG	NG	Dentated
Kgiku et al <sup>27</sup>	Croatia	10 (5/5)	73±13.6 (46-94)	20	100	NG	14.5	Dentated

Conversely, ten cross-sectional studies: five Asian (Chan & Wang, 2011; Mardinguer et al, 2007; Jung et al, 2011; Kim et al, 2011; Yang & Kye, 2014), three European (Güncü et al, 2011; Ilgüy et al, 2013; Rosano et al, 2011), and two American (Elian et al, 2005; Anamali et al, 2013), published during the last decade, met the eligibility criteria. These reports gather a total of 1,647 patients and 2,740 MS (study

unit). Three of these papers obtained their images from SLS preoperative studies (Elian et al, 2005; Güncü et al, 2011; Rosano et al, 2011); four reports included CT/CBCT explorations made before implant insertion in the posterior maxilla (Kang et al, 2013; Mardinger et al, 2007; Jung et al, 2011; Kim et al, 2011; Yang et al, 2014); and the remaining two articles used images of patients with subsinusal edentulism retrieved from the files of maxillofacial radiology units (Anamali et al, 2013; Ilgüy, 2013) (Table 2).

**Table 2.** Characterization of patients and studies considered in the meta-analysis

Author, year	Country	n (M/F)	Age X±SD (Mn-Mx)	Maxillary sinus (n)	Type of exploration	Prevalence (CI 95%)	PSAA Diameter (X±SD)	Distance PSSA-alveolar crest* (X±SD)	QS
Elian et al	USA	50 (-)	(-)	100	CT	52.9 (43.12-62.68)	-	16.4±3.5	4
Mardinger et al	Israel	104 (35/69)	52.9 (24-76)	208	CT	55 (48.24-61.76)	-	16.9±4.4	4
Rosano G	Italia	100 (-)	53.5 (29-78)	200	CT	47 (40.08-53.92)	-	11.2±2.9	4
Kim et al	Korea	200 (-)	57.7 (45-65)	400	CT	52 (47.10-56.90)	1.5±0.4	15.4±4.0	3
Güncü et al	Turkey	121 (49/72)	48.7±11.8	242	CT	64.5 (58.47-70.53)	1.3±0.5	18.0±4.9	5
Jung et al	Korea	250 (159/91)	57.1 (33-83)	250	CBCT	52.8 (46.61-58.99)	-	14.7±4.0	4
Anamali et al	USA	254 (120/134)	57.6 (20-87)	254 254	CBCT CBCT	94.4 (91.57-97.23) 91 (87.48- 94.52)	-	-	4
Ilgüy et al	Turkey	135 (55/80)	43.1±17.5	116	CBCT	75.9 (68.12-83.68)	0.9±0.2	16.8±3.4	4
Kang et al	Korea	150 (90/60)	49.35 (23-86)	150	CBCT	90 (85.20-94.80)	1.18±0.4	17.03±3.5	4
Yang & Kye	Korea	283 (186/97)	57.1 (18-84)	566	CT	36.5 (32.51-40.62 )*	-	18.3±0.5*	4

(\*) Data obtained from the authors; QS: quality score

The radiographic studies included in this meta-analysis have shown a pooled prevalence of PSAA in the lateral wall of the maxillary sinus of 62.02 (46.33 – 77.71) (Table 3). Six of these studies used CT scanning to identify the intraosseous

anastomosis (Elian et al, 2005; Mardinguer et al, 2007; Kim et al, 2011; Güncü et al, 2011; Yang & Kye, 2014) whereas the other four employed CBCT technology (Jung et al, 2011; Kang et al, 2013; Anamali et al, 2013; Ilgüy et al, 2013). These latter studies have reported higher frequencies of PSAA detection (pooled prevalence of 78.1 (95%CI=61.2-94.9), ranging from 52.8% to 94.4%), (Jung et al, 2011; Anamali, 2013) in comparison to CT studies pooled prevalence 51.19 (42.33 - 60.05).

**Table 3.** Pooled prevalence (PP) and 95% confidence intervals (CI) of the PSAA in the lateral wall of the MS.

	N° of studies	PP (95% CI) fixed effects	PP (95% CI) Random effects	Ri *	Q test p-value
All studies	10	73.10 (71.65 - 74.55)	62.02 (46.33 - 77.71)	0.99	0.00001
< 16mm	3	51.06 (47.70 - 54.42)	51.06 (47.70 - 54.42)	0.00	0.41
≥ 16mm	6	60.69 (58.33 - 63.06)	62.48 (43.62 - 81.34)	0.98	0.00001
TC	6	48.70 (46.35 - 51.05)	51.19 (42.33 - 60.05)	0.93	0.00001
CBCT	4	88.11 (86.26 - 89.95)	78.12 (61.25 - 94.98)	0.99	0.00001

\* Proportion of total variance due to between-study variance

Radiographic studies using conventional CT revealed an average gauge of the artery higher than reported when CBCT was used. More than 60% of the sinuses studied with CBCT showed PSAAs <1mm diameter (Kang et al, 2008; Yang & Kye, 2014), this proportion being lower for CT-studied sinuses (Mardinguer et al, 2007; Kim et al, 2011; Güncü et al, 2011; Rosano et al, 2011).

A wide range of average distances from the artery to the osseous crest (11.2 to 18.3mm) have been reported (Rosano et al, 2011; Yang & Kye, 2014). Except for the three studies with distances lower than 16mm (Jung et al, 2011; Kim et al, 2011; Rosano et al, 2011), heterogeneity between studies was large. As previously explained, we considered the random effects estimates to be the only ones acceptable.

Only four studies report on the mediolateral position of the PSAA in the sinus wall: three of them describe a fully intraosseous path for the artery (Kang et al, 2013; Güncü et al, 2011; Ilgüy et al, 2013) while the other frequently finds the vessel in an intrasinusal position between the Schneider's membrane and the sinus bony wall (Jung

et al, 2011). In all the series considered, the superficial position of the artery (on the outer cortex of the lateral sinus wall) was the least frequently reported location, with percentages ranging from 5.2% to 7.7% of the sinuses studied (Jung et al, 2011; Ilgüy et al, 2013).

### **3.1.6. Discussion**

Our results demonstrate that preoperative assessment with CBCT permits a more frequent and more effective detection of PSAA than conventional CT. As no clinical trials are available, the data considered in this meta-analysis were obtained from large case-series with an unlikely selection bias. Some of these studies have limitations related to the lack of control for confounding factors, such as age (Elian et al, 2005), gender (Elian et al, 2005; Kim et al, 2011; Rosano et al, 2011), or ethnicity, which may compromise their internal validity. Also, the intrasinusal location of the artery may hinder radiologic detection and act as an additional confounding factor (Rosano et al, 2011).

The lesser radiologic detection of PSAAs (present in 100% of specimens) may be related to their small diameter (Mardinguer et al, 2007; Rosano et al, 2009). The average gauge of the CT-detected arteries is markedly higher than reported from CBCT studies, which may mean that only larger arteries are detected from this approach (Kim et al, 2011; Güncü et al, 2011). CBCT has proven to deliver better sensitivity and cost-effectiveness for PSAA detection and it is recommended as a dose-sparing alternative to conventional CT for maxillofacial imaging (Ilgüy et al 2013).

Despite of the need for a preoperative PSAA assessment, the relevance of vascular damage during antrostomy is size-dependent: the section of a small (<1mm) vessel has a negligible surgical impact (Mardinguer et al, 2007) while larger diameters may hamper visualization and compromise the procedure (Zijderfeld et al, 2008). Vessels >3mm may be ligated to prevent severe iatrogenia (Testori et al, 2010; Rosano et al, 2011). In this sense, the studies considered in this meta-analysis report an average artery size ranging from 0.9 to 1.5mm (Kim et al, 2011; Ilgüy et al, 2011); larger diameters being linked to the male gender (Kang et al, 2013) and thicker bony walls

(Kang et al, 2013), with a controversial age influence (Mardinguer et al, 2007; Testori et al, 2010; Kang et al, 2013).

These circumstances highlight the importance of the distance between the PSAA and the bony crest when designing an antrostomy (Solar et al, 1999). Average reported values (although grouped) (Elian et al, 2005; Mardinguer et al, 2007; Jung et al, 2011; Kim et al, 2011; Ilgüy et al, 2013; Kang et al, 2013) are scattered within a wide range of distances (2.8-31.7mm) probably due to anatomical variations and different vertical ridge dimensions (Güncü et al, 2001; Kang et al, 2013). The PSAA position should also be taken into account, particularly if partially intraosseous and located on the inner side of the lateral bony wall, to avoid vascular injuries during membrane detachment (Chan & Wang, 2011). This situation is reported to occur in about 13% to 63.8% of the sinuses analysed (Jung et al, 2011; Ilgüy et al, 2013).

Although no significant differences between piezosurgery and conventional rotary instruments in terms of visibility, surgical time, membrane perforation and patient expectations is noted (Delibasi & Gurler, 2013; Seoane et al, 2013), the use of piezosurgery may be particularly recommended for sinuses with higher gauge PSAA anastomosis.

Within the inherent limitations and potential bias of the studies considered in this meta-analysis, it is concluded that the prevalence of PSAA detection in the sinus lateral bony wall is higher when CBCT explorations are used, compared with scores for conventional CT radiographic studies. Still, additional comparative studies that control for potential confounding factors are needed to ascertain the actual diagnostic value of radiographic explorations for assessing the PSAA prior to SLS procedures

## **3.2. CHAPTER II: Detection of alveolar antral artery by cone beam computed tomography. Observational study and modelization of associated factors.**

### **3.2.1. Abstract**

Background: Surgical damage of the AAA is the second most common complication of SLS, and may result in mobilisation of the graft and membrane perforations.

The aims of the study were to assess artery detection by CBCT and to describe explanatory models useful in surgical planning.

Methods: A retrospective observational study of CBCT explorations at the first upper molar area was undertaken. The modelling of the probability for detecting AAA was carried out using logistic generalized additive models (GAM). The capacity for discriminating between artery detection vs. no detection was assessed by means of ROC curves.

Results: A total of 466 sinuses were studied. Univariate models showed the probability of artery detection is linked to the sinus width and the thickness of the lateral bony wall, together with the shape and height of the osseous crest. The probability for AAA detection increased steadily until the thickness of the bony wall reached 6mm.

The multivariate models behaved as good discriminators for AAA detection, particularly in female patients, showing an area under the curve (AUC) of 0.85, whereas those models considering patients altogether, and including only male patients offered slightly lower values (AUC=0.79).

Conclusions: the probability of artery detection by CBCT is influenced by patient gender (higher in males and for narrow sinuses) and increases with the thickness of the sinus lateral bony wall and the height of the residual alveolar ridge. Particularly for women, the thickness of the ridge at the basal level seems to improve the explanatory model for artery detection.

**Key words:** cone-beam computed tomography, blood vessels, sinus floor augmentation, intraoperative complications.

### 3.2.2. Introduction

SLS by lateral approach is a safe and predictable procedure for augmenting bony tissue to allow implant placement (Chen et al, 2009). However, certain potential complications must be taken into account either intra-operatively (Schneider's membrane perforation, haemorrhage from the AAA, and osteomeatal complex obstruction) or post-operatively (sinus congestion, graft mobility, acute sinusitis, and cyst formation) (Maridati et al, 2014).

Accidental bleeding secondary to surgical damage of AAA is the second most common complication of SLS (Maridati et al, 2014; Varela-Centelles et al, 2015). Observational studies and case series highlight that up to 20% of major bleeding events during SLS surgery are due to AAA damage (Flanagan, 2005; Elian et al, 2005). This damage may indirectly result in postponement of the surgery, a slower surgical procedure, reduction of blood supply, mobilisation of the graft, and also in an increase in the frequency of membrane perforations (Maridati et al, 2014).

The AAA is an anastomosis of the PSAA and the IOA which has been repeatedly identified by dissection in 100% of the lateral sinus walls of cadavers (Soltar et al, 1999; Hur et al, 2009; Rosano, 2009; Sato, 2010; Kqiku et al, 2013). The AAA can follow either a straight or a U-shaped course in the anterolateral wall of the sinus, whose closest point to the alveolar crest is at the site of the first or second molar (Mardinger et al, 2007; Jung et al, 2011). Its relationship with the bony wall is also variable, being most commonly completely intraosseous and rarely (less than 8%) superficial, on the outer cortex under the periosteum of the sinus lateral wall (Jung et al, 2011). This circumstance may condition the surgical approach, making careful planning of the surgery of particularly importance, where correct identification of the AAA is mandatory to avoid undesired complications (Zijderveld et al, 2008).

Although CBCT has proven to be superior to CT in identifying the AAA (Varela-Centelles et al, 2015), sometimes this artery is not identified. This lack of detection does not mean AAA does not exist; it may be due either to a small diameter (<0.5mm) or to a intrasinus or superficial position of the vessel (Mardinger et al, 2007; Rosano et al, 2011).

A recent meta-analysis reported that the pooled prevalence of AAA detected by CBCT was 78.12 (95%CI: 61.25-94.98), (Varela-Centelles et al, 2015). Its authors warned about the poor internal validity and potential bias of some reports on this topic - mostly related to a lack of control for potential confounding factors, such as age, gender, or ethnicity (Elian et al, 2005; Rosano et al, 2011; Kim et al, 2011) which may have compromised their results.

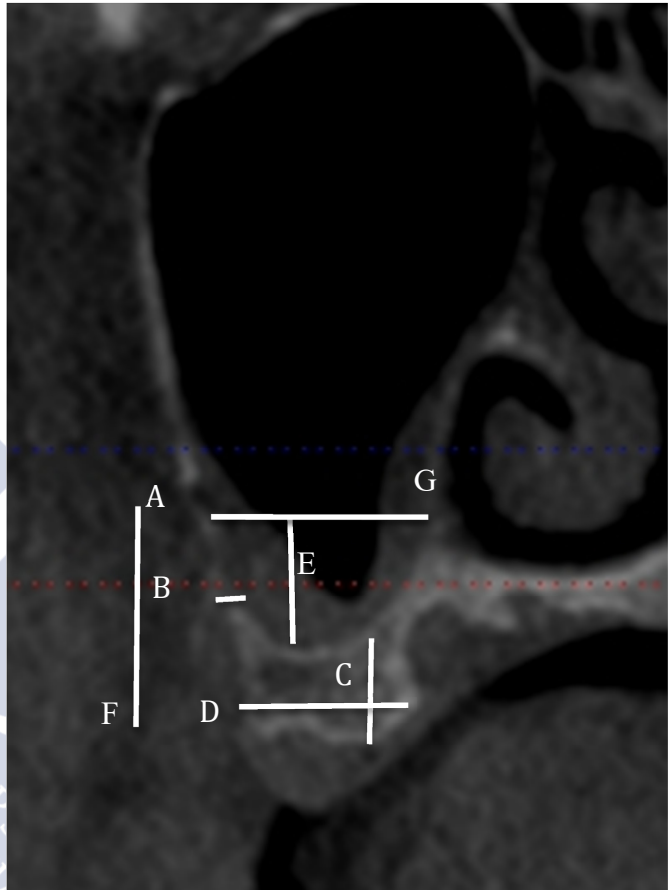
There are currently limited studies on AAA detection which take into account these confounding factors; the aims of this investigation were to render information on the prevalence of AAA detection by CBCT, to study the variables related to its detection while controlling for potential confounding factors, and also to describe explanatory models to help in surgical planning for these patients.

### **3.2.3. Methods and materials**

A retrospective observational study was undertaken from March to November 2015 at the Radiology Unit of the School of Medicine and Dentistry of the University of Santiago de Compostela (Spain) with the approval of the university's Ethics Committee and in full accordance with the Declaration of Helsinki. After obtaining informed consent, CBCTs were selected by means of a database manager and selected according to the following inclusion criteria: CBCT explorations performed for surgical planning of implant-supported prosthesis in either maxillary edentulous or subsinusally edentulous patients, as well as for patients scheduled for replacement of a single upper first molar. Exclusion criteria were poor image quality, sinus disorders, or previous experience of sinus surgery or grafting.

All patients were explored by means of a cone beam CT (I-CAT, 17-19. Imaging Sciences International, 1910 North Penn Toad, Hatfield, USA) with its I-CAT software (Imaging Sciences International) set at a resolution of 0.3 voxels with 8.9 seconds of capture time. The area of the first upper molar was selected for performing the coronal sections because of the proximity of the artery to the bony crest, (Rodella et al, 2010) which is of particular interest for surgical planning.

Two observers, experts in Oral Surgery (ML & AG), elicited a high concordance in AAA detection (Kappa = 0.92) and used the linear measurement tool of the I-CATVision device to measure quantitative variables. The relative uncertainty (standard deviation of the measurement divided by its mean and expressed as a percentage from 0% to 100%) was chosen for determining the error of these observations. The variables assessed (with its relative uncertainty) were: thickness of the lateral sinus wall (0.25%), height of the residual alveolar ridge (0.42%), width of the residual alveolar ridge (basal level) (0.04%), width of the residual alveolar ridge (crestal level) (1.43%), distance from AAA to sinus floor (0%), distance from AAA to alveolar crest (0%); and MS width measured at 15mm from the ridge crest (distance from medial to the lateral sinus wall) (0.01%) (Chan et al, 2014), (Figure 7).



**Figure 7:** A: Antral Alveolar Artery (AAA), B: thickness of the lateral sinus wall, C: height of the residual alveolar ridge, D: width of the residual alveolar ridge, E: distance from AAA to sinus floor, F: distance from AAA to alveolar crest, G: maxillary sinus width.

Patients' age was also considered as a continuous variable. The main categorical variable studied in this investigation (outcome) was “detection vs no detection of the AAA's bony canal in the lateral sinus wall”. Additional potentially-related co-variables, such as gender, pattern of tooth loss (maxillary edentulous, subsinusual edentulous, or absent upper first molar), position of the artery (fully intraosseous, intrasinusual -between the Schneiderian membrane and the sinus bony wall-; or superficial -on the outer cortex of the lateral sinus wall). The type of residual bony crest was classified according to Cawood & Howell (1988) as class II: immediately post extraction; class III: well-rounded ridge; class IV: knife-edge ridge; class V: flat ridge; and class VI: depressed ridge form.

### **Statistical analysis**

The MS was considered as the study unit. The results for categorical variables were expressed as frequencies, whereas quantitative variables were defined by their median and mean as statistics for central trend, and by the inter-quartile range as a spread indicator.

The modelling of the probability for detecting AAA was undertaken using logistic generalized additive models (GAM) (Wood, 2011). This approach permits the modelling of the effect of co-variables in a flexible way, as the response variable is dichotomous.

Univariate models have been adjusted for each of the independent variables. Once the best multivariate model was automatically selected and adjusted for males and females, the absence of concurvity was checked. The capacity for discriminating between artery detection vs. no detection was assessed by means of ROC curves.

All the analyses were carried out with the free software R. (R Core Team, 2016) using the mgv package (Wood, 2006) for GAM modeling, and ROCR (Sing et al, 2005) for ROC analysis. Inter-observer concordance for two categories was calculated by means of EPIDAT 3.1 statistical package (Programa para Análisis Epidemiológico de Datos Tabulados. Xunta de Galicia. Santiago de Compostela, Spain).

#### **3.2.4. Results**

A total of 466 MS were studied, 198 males (42.5%) and 268 females (57.5%), with a median age of 57 years (IQR: 49.25-65). CBCT explorations identified the AAA in 240 sinuses (51.5%). The median width of the sinus lateral bony wall was 1.80mm (IQR: 1.5-2.5), with the AAA most commonly running a fully intraosseous course within this wall (48.7%) with a diameter ranging from 1 to 2mm in most cases (67.5%).

The predominant subsinusal bone resorption patterns were the “well-rounded” and “flat ridge” forms (class II: 7.2%; class III: 38.3%; class IV: 13.0%; class V: 24.2%; class VI: 17.3%), with a ridge height of 7.10 mm (IQR: 4.9-9.7) (Table 4).

Table 4: Main features of the sample studied

Variables	n	(%)
<b>Gender</b>		
Male	198	42.48
Female	268	57.52
<b>AAA detection</b>		
No	226	48.49
Yes	240	51.51
<b>AAA position</b>		
Fully intraosseous	117	48.75
Superficial	8	3.33
Intrasinusal	115	47.91
<b>AAA diameter</b>		
≤ 1 mm	47	19.58
>1 ≤ 2mm	162	67.50
>2 mm	31	12.91
<b>Pattern of edentulousness</b>		
Fully edentulous maxilla	59	12.6
Subsinusal edentulousness	329	70.6
Upper first molar missing	78	16.7
	<b>Mean</b>	<b>Median (IQR)</b>
<b>Age (years)</b>	56.88	57.00 (49.25-65.00)
<b>Thickness of the lateral sinus wall (mm)</b>	2.31	1.80 (1.50-2.50 )
<b>Height of the residual alveolar ridge (mm)</b>	7.44	7.10 (4.90-9.70)
<b>Width of the residual alveolar ridge (basal level) (mm)</b>	10.06	10.10 (8.20-11.90)
<b>Width of the residual alveolar ridge (crestal level) (mm)</b>	6.62	6.40 (4.70-11.90)
<b>Distance from AAA to sinus floor (n=240) (mm)</b>	7.66	7.10 (5.20-9.70)
<b>Distance from AAA to alveolar crest (n=240) (mm)</b>	15.26	14.90 (12.20-17.50)
<b>Maxillary sinus width (mm)</b>	12.60	12.40 (10.05-14.80)

Univariate models have shown that the probability of artery detection is linked to the sinus width and to the thickness of the lateral bony wall, as well as to the shape and height of the osseous crest. The probability for AAA detection increased steadily until the thickness of the bony wall reached 6mm. Beyond this point, the probability decreased. A decreasing trend in the chance of detection was also observed when the sinus width increased. Conversely, the chances of identifying the AAA increased with the height of the residual crest: post-extraction, rounded crests were significantly linked to AAA detection when compared to flat and depressed ridges (Table 5).

Table 5. Univariate logistic models

Univariate linear logistic models	Estimate (β)	Standard Error	Z value	p-value	Degrees of freedom (df)	Model's Chi Square	Model's p-value
<b>Gender</b>					1	2.79	0.09
Intercept	0.75	0.16	4.51	6.41e-06			
Female	-0.36	0.21	-1.67	9.44e-02			
<b>Pattern of edentulousness</b>					2	0.53	0.06
Intercept	0.15	0.24	0.61	0.53			
Fully edentulous maxilla vs upper first molar missing	0.60	0.39	1.50	0.13			
Subsinusal edentulousness vs upper first molar missing	0.66	0.28	2.35	0.01*			
<b>Classification of posterior maxilla</b>					4	16.96	0.00
Intercept	-0.09	0.24	-0.37	0.70			
Class IV vs Class VI	0.54	0.38	1.42	0.15			
Class V vs Class VI	0.38	0.32	1.16	0.24			
Class II vs Class VI	1.34	0.52	2.56	0.01**			
Class III vs Class VI	1.11	0.31	3.58	0.000***			
Class V vs Class IV	-0.16	0.36	-0.46	0.64			
Class II vs Class IV	0.79	0.54	1.45	0.14			
Class III vs Class IV	0.56	0.34	1.63	0.10			
Class II vs Class V	0.96	0.50	1.89	0.05			
Class III vs Class V	0.73	0.28	2.59	0.00***			
Class III vs Class II	-0.22	0.50	-0.45	0.64			
<b>Univariate GAM logistic models</b>				Explained deviance (%)	Effective degrees of freedom (edf)	Model's Chi square	Model's p-value
<b>Age (years)</b>				0.85	1.67	2.53	0.18
<b>Thickness of the lateral sinus wall (mm)</b>				5.16	1.92	22.57	2.59e-05***
<b>Height of the residual alveolar ridge (mm)</b>				1.20	1.29	6.40	0.04*
<b>Width of the residual alveolar ridge (basal level) (mm)</b>				0.99	1.75	4.41	0.14
<b>Width of the residual alveolar ridge (crestal level) (mm)</b>				1.26	1.79	3.64	0.13
<b>Maxillary sinus width (mm)</b>					1.00	34.69	3.85e-09***

The best multivariate model showed an explained deviance of 21%, and included gender, pattern of edentulousness, sinus width, thickness of the sinus lateral bony wall, and shape and height of the ridge (Logit  $\{P(\text{Detection}|X_i)\} = \alpha + \beta_1 \text{ gender} + \beta_2 \text{ type of edentulousness} + \beta_3 \text{ ridge shape} + f_1(\text{ridge height}) + f_2(\text{thickness of lateral bony wall}) + f_3(\text{sinus width})$ ), where  $f_1$  to  $f_3$  represent smooth functions of covariates.

When adjusting for gender, the best multivariate model for females was (Logit  $\{P(\text{Detection} | X_i)\} = \alpha + \beta_1 \text{ type of edentulousness} + \beta_2 \text{ ridge shape} + f_1(\text{width of the ridge at the basal level}) + f_2(\text{ridge height}) + f_3(\text{thickness of the lateral bony wall}) + f_4(\text{sinus width})$ ), which explains a deviance of 31.2% (Table 6).

In women, rounded crests (class III) are linked to a significantly higher probability of AAA detection when compared to other resorption patterns. Furthermore, the width of the ridge at the basal level was shown to be significantly associated with artery detection; the chance increasing for values over 5mm. A similar situation occurred when the thickness of the lateral bony wall was considered, where the probability of AAA detection increased with thicknesses up to values about 4mm, to decrease beyond this score, although the confidence interval was too wide to consider this effect as significant (Figure 8). There was a very clear association between sinus width and AAA detection, with chances for artery identification markedly diminishing as the sinus width increased, being just about zero for widths over 20mm (Figure 8, Table 6).

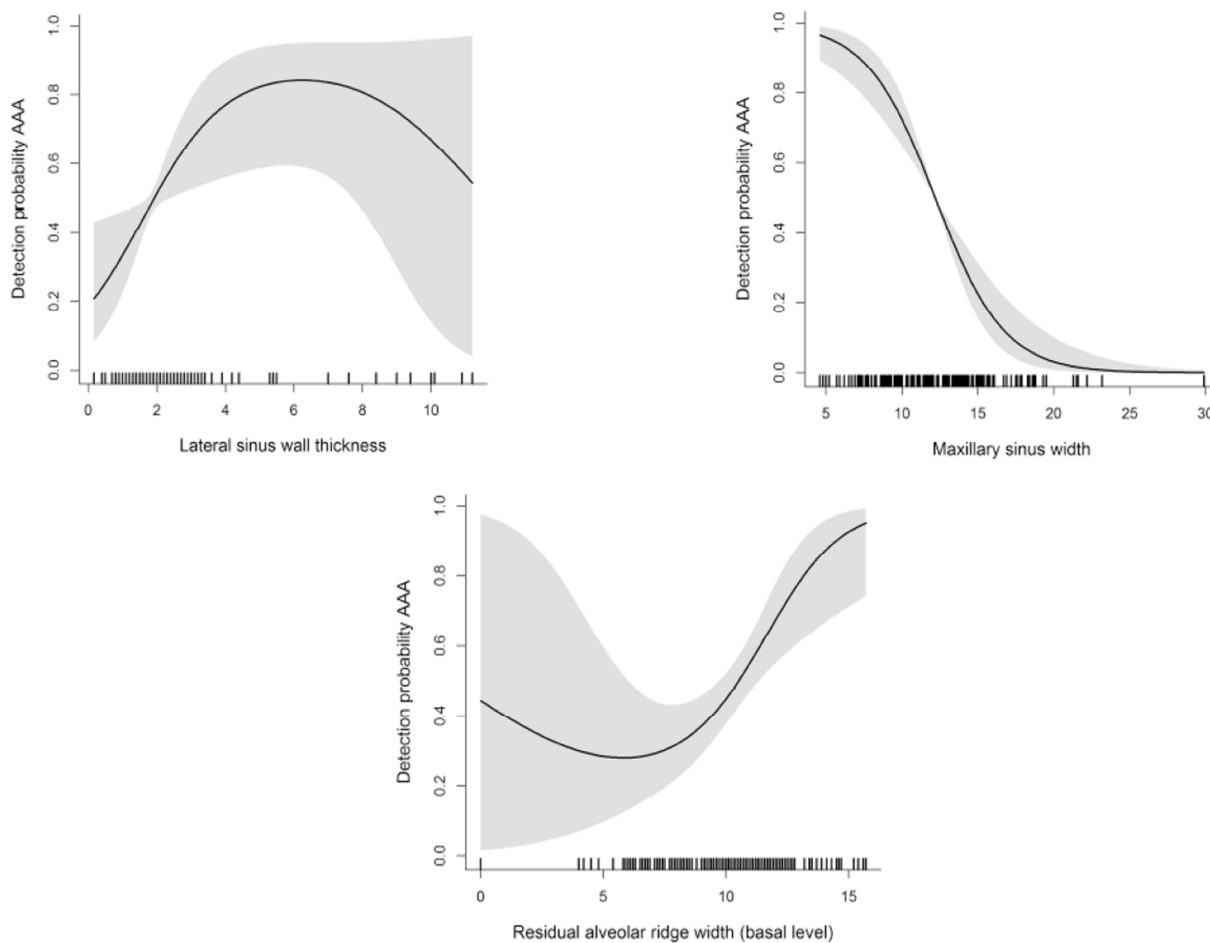


Figure 8: Artery detection probability for female patients

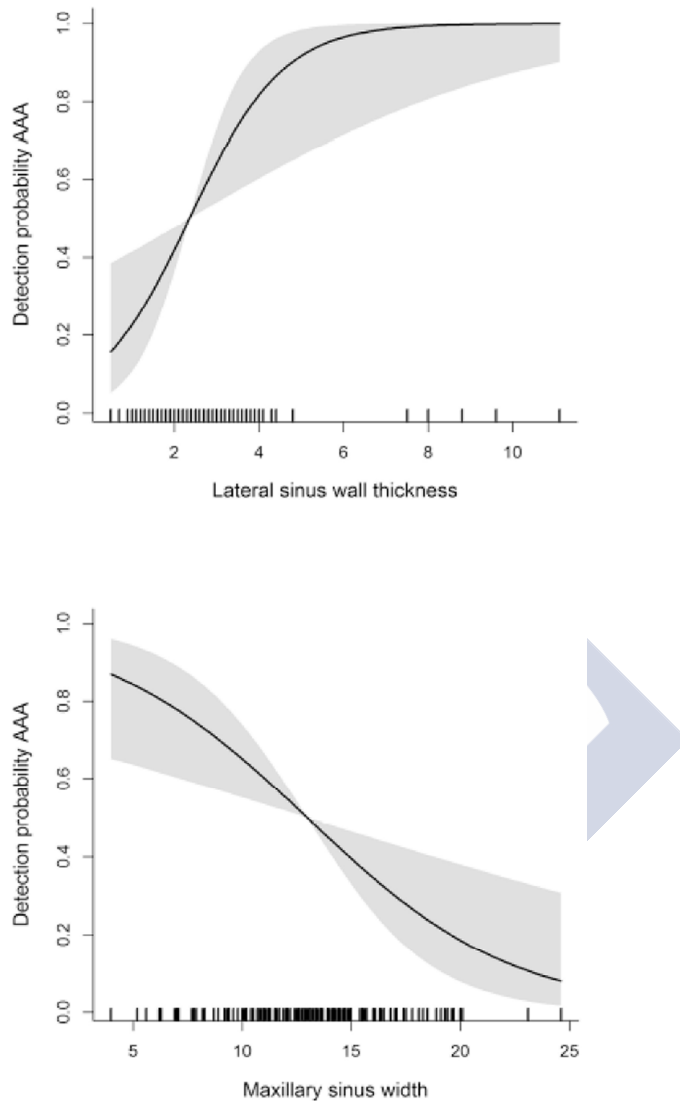


Table 6. Multivariate model

Multivariate model by gender	Female. (percentage of deviance explained by the model = 31.2%)				Male (percentage of deviance explained by the model = 22%)			
	Estimate (β)	Std. Error	Z value	p-value	Estimate (β)	Std. Error	Z value	p-value
<b>Pattern of edentulousness</b>								
Intercept	-0.69	0.77	-0.90	0.36	-0.91	0.72	-1.27	0.20
Fully edentulous maxilla vs upper first molar missing	1.16	0.85	1.36	0.17	1.54	0.67	2.29	0.02**
Subsinusal edentulousness vs upper first molar missing	0.88	0.47	1.86	0.06	1.82	0.54	3.33	0.00**
Subsinusal edentulousness vs fully edentulous maxilla	-0.27	0.74	-0.36	0.71	0.28	0.54	0.51	0.60
<b>Classification of posterior maxilla</b>								
Class IV vs Class VI	0.19	0.85	0.22	0.82	0.63	0.84	0.75	0.45
Class V vs Class VI	0.43	0.71	0.60	0.54	0.23	0.63	0.37	0.71
Class II vs Class VI	-0.05	1.07	-0.05	0.95	3.05	1.33	2.29	0.02**
Class III vs Class VI	1.57	0.78	1.99	0.04*	1.46	0.78	1.86	0.06
Class V vs Class IV	0.23	0.69	0.34	0.73	-0.39	0.76	-0.51	0.60
Class II vs Class IV	-0.25	0.99	-0.25	0.79	2.42	1.33	1.81	0.06
Class III vs Class IV	1.37	0.70	1.95	0.05*	0.82	0.74	1.11	0.26
Class II vs Class V	-0.49	0.87	-0.56	0.57	2.82	1.27	2.21	0.02**
Class III vs Class V	1.13	0.50	2.24	0.02*	1.22	0.65	1.87	0.06
Class III vs Class II	1.63	0.82	1.96	0.04*	-1.59	1.21	-1.30	0.19
Flexible part of the model (smooth terms)	Degrees of freedom (df)	Effective degrees of freedom (edf)	Chi square	Model's p-value	Effective degrees of freedom (edf)	Degrees of freedom (df)	Chi square	Model's p-value
Thickness of the lateral sinus wall	1.76	1.94	7.01	0.03*	1	1	7.67	0.00**
Height of the residual alveolar ridge	1.80	2.27	5.32	0.11	1	1	3.42	0.06
Maxillary sinus width	1.00	1.00	30.47	3.39e-08***	1	1	8.97	0.00**
Width of the residual alveolar ridge (basal level)	1.76	1.94	11.16	0.00**				

For males, the best model explained a deviance of 22% and included the pattern of edentulism (Logit {P (Detection |X<sub>i</sub>) } = α + β<sub>1</sub> type of edentulousness + β<sub>2</sub> ridge shape + f<sub>1</sub> (ridge height) + f<sub>2</sub> (thickness of the lateral bony wall) + f<sub>3</sub> (sinus width)). Thus, the chances for AAA detection are higher in fully edentulous patients, in comparison to those with only the first upper molar missing. The probability of detection increased along with the width of the sinus lateral bony wall up to values close

to 4mm for females, with higher chances in males. The width of the sinus also showed an inverse relationship with chances of AAA detection, but the probabilities decreased in a less pronounced way than for females (Figure 9).



**Figure 9:** Artery detection probability for male patients

The multivariate models suggested in this study have behaved as good discriminators for AAA detection, particularly in female patients, showing an area under the curve of 0.85. Models, which consider patients altogether, or including only male patients, offered slightly lower values (AUC=0.79), which are within the limit of being considered a good discriminator.

### 3.2.5. Discussion

Despite the relevance of pre-surgical identification of AAA for SLS and other procedures involving the lateral wall of the MS, such as Le fort I osteotomies, or Caldwell-Luc surgery (Rahpeyma & Khajehahmadi, 2014), very few isolated studies have focused on the determinants of radiologic AAA detection. In this sense, and regardless of the extra-osseous position of the artery, only the small diameter of the vessel lumen, the technique employed (CBCT vs CT), and the skills and experience of the observers seem to explain the low detection rates of CBCT and CT (62.0%; 95%CI: 46.33-77.71) when compared to anatomical findings (Jung et al, 2011; Maridati et al, 2014) which acknowledged 100 % AAA presence with a partially intra-osseous course (Solar et al, 1999; Kqiku et al, 2013). Age and gender have also been related to the radiological identification of AAA, although this relationship is based upon poorly consistent results (Mardinger et al, 2007; Kim et al, 2011).

Reports on CBCT, AAA detection described probabilities ranging from 35% to 90% (Kang et al, 2013). This wide range may be due to the high percentage of males in the latter study. Our results reveal the presence of the AAA in 51.5% of the cases, including 57.5% females. As previously reported in the literature, the AAA mostly described a fully intraosseous course within the lateral wall of the sinus (Kang et al, 2013; Güncü et al, 2011; Ilgüy et al, 2013). The intrasinusal location of the artery, between the sinus membrane and the lateral wall (where a small concavity can be seen), was found to be the second most frequent in our series (Rosano et al, 2009). The anatomically described absence of a bony layer between the AAA and the sinus membrane may influence the surgical handling of AAA in this position, particularly during the procedure of membrane detachment (Rosano et al, 2009; Valente, 2015). In our sample, the superficial position of the artery, just underneath the periosteum with a radiologically visible indentation in the lateral wall of the sinus, was a less frequent one (3.3%), just less than the reported prevalence for this position in the literature (Güncü et al, 2011, Kang et al, 2013; Ilgüy et al, 2013). The AAA can also describe a fully extraosseous course (Maridati et al, 2014), but in these cases the artery lies within the flap, and the risk for haemorrhage would be associated with the incision, but not with the antrostomy (Rodella et al, 2010).

The results linked to the diameter of the AAA have been traditionally presented as categorical variables. This is important as the risk for arterial damage during anrostomy is size-dependent (Varela-Centelles et al, 2015). Hence, damage to a small AAA (< 1mm) (about 19.5% in our series and ranging between 13.9%-55.3% in the literature (Rosano et al, 2011; Kim et al, 2011) has a negligible surgical impact. Damage to larger arteries may hamper visualization and hinder the surgical procedure (Zijderveld et al, 2008). The frequency of AAA diameters between 1 and 2mm is reported to extent between 22.1% and 64.9% (Mardinger et al, 2007; Kim et al, 2011). Arteries with a diameter exceeding 2mm are likely to produce sufficient bleeding to interfere with the placement of the bony graft, becoming a real surgical complication (Rosano et al, 2011). In our sample, 12.9% fell within this category, which ranges from 4.3% to 21.3% in other case series (Varela-Centelles et al, 2015). Vessels larger than 3mm should be avoided or ligated to prevent severe iatrogenesis (Testori et al, 2010). The position of the AAA with respect to the alveolar ridge also influences osteotomy, and this spatial relationship varies widely in the literature, from 11.2mm (Yang et al, 2014) to 18.3mm, (Rosano et al, 2011) and it is most likely due to variations in the height of the residual ridge height of about 7.7mm. Therefore, pre-surgical awareness of the variables is paramount to adequately design the osteotomy for SLS procedures.

The main strength of the current study relies on its being the first to focus on controlling the potential risk factors and detailing explanatory models for the detection of AAA. The large sample analysed in our study is consistent with previous reports in terms of age and gender distribution, as well as in artery diameter and position. The inclusion criteria for assessing patients for dental implant treatment makes selection bias less likely in our investigation (Varela-Centelles et al, 2015).

The influence of age in AAA diameter is equivocal (Mardinger et al, 2007), and there was no association with its radiological detection, neither in previous reports (Kim et al, 2011; Ilgüy et al, 2013) nor in our study. On the other hand, gender was found to be an explanatory variable in the multivariate model influencing artery detection. Larger diameters and higher detection rates were found amongst males, (Kim et al, 2011) which implies a greater chance of intra-operative bleeding for this group in comparison to females (Kang et al, 2013). The thickness of the sinus lateral bony wall

also behaved as an explanatory variable, as larger AAAs were identified in thicker walls (Maridati et al, 2014; Bernardi et al, 2015). Therefore, when facing a thick wall, the risk for bleeding should be taken into account (Kang et al, 2013). However, the use of flexible models demonstrate that this association is not linear and the chances of detection rapidly increase up to 6mm thickness and then decrease beyond this value. The width of the MS also influences the surgical difficulty of SLS (Chan et al, 2014) and has an effect on the probability of detecting AAA by CBCT. These chances significantly diminish when the distance between the lateral and medial walls of the sinus increase, particularly in women. Although our sample shows predominantly narrow sinuses (<14mm width), the AAA was almost undetectable in wide sinuses (>20mm). The probability of detecting AAA is higher for well-rounded ridges with an adequate height, and it increases with height for this particular ridge shape.

Bearing in mind the CBCT, AAA detection rate and its capability for identifying arteries >0.5mm –which may cause relevant bleeding during antrostomy with conventional rotary instruments-, it is recommended to undertake a careful surgical planning with CBCT explorations, and to use piezoelectric instruments to minimise surgical damage to the vessel (Wallace et al, 2007; Valente, 2015; Seoane et al, 2013).

### **3.2.6. Conclusions**

The probability of AAA detection by CBCT is influenced by patient's gender (higher in males and for narrow sinuses) and increases with the thickness of the sinus lateral bony wall and height of the residual alveolar ridge. Particularly for women, the thickness of the ridge at the basal level would seem to improve the explanatory model for AAA detection. With these findings in mind, we would suggest assessment and control for these variables in future studies on this topic.

### **3.3. CHAPTER III: Distance of the alveolar antral artery from the alveolar crest. Related factors and surgical considerations in sinus floor elevation.**

#### **3.3.1 Abstract**

Objectives: to identify and model the variables related to patients at risk of iatrogenic bleeding during SLS whose AAAs are located within 15mm of the bony crest.

Study design: retrospective observational study

Results: A total of 240 MS were studied (46.25% males) with a median age of 58 years (IQR: 52-66). Univariate models showed that the chances of an AAA-alveolar crest distance  $\leq 15$ mm increases in wider sinuses with lower, subsinusally edentulous crests. When distance is considered as a continuous variable, the best multivariate model showed an explained deviance of 67% and included the AAA diameter, distance AAA-sinus floor, sinus width, as well as the shape, height and width of the residual ridge. Thinner AAAs are found closer to the crest (within the  $\leq 15$ mm safe distance).

Conclusions: Whilst bearing in mind the inclusion criteria and limitations of this investigation, the findings show a high proportion of maxillary sinuses where the AAA follows a course close to the alveolar crest ( $\leq 15$ mm), which was classically considered a safe distance for SLS. This position is related to the presence of an atrophic crest (depressed ridge form) and wide MS where the distance of the vessel to the floor of the sinus is small. This information may permit better surgical planning of SLS procedures.

**Key words:** cone-beam computed tomography, blood vessels, sinus floor augmentation, intraoperative complications.

#### **3.3.2. Introduction**

Although SLS by lateral approach is a safe and predictable surgical technique for gaining bony tissue for implant placement, it is not without risk of intra- and post-

operative complications (Chiapasco et al, 2009; Maridati et al, 2014). The second most frequent of these complications (the first being sinus membrane perforation) is bleeding collateral to surgical damage to the AAA during antrostomy (Maridati et al, 2014).

AAA is an anastomosis of the PSAA and the IOA located at the anterolateral wall of the sinus taking a variable course, which supplies the Schneiderian membrane, sinus wall, and the periosteum (Varela-Centelles et al, 2015). It also contributes to graft integration and to the healing of the surgical wound (Maridati et al, 2014).

Careful surgical planning using CBCT has been advocated in an attempt to minimise bleeding complications during SLS. Yet, AAA detection rate by CBCT is 78.1% (95%CI=61.2-94.9), and it has proven unable to disclose the presence of small arteries (<0.5mm) and those with a intrasinus or fully extraosseous course (Maridati et al, 2014; Varela-Centelles et al, 2015).

In any case, the vascularity of the lateral sinus wall varies widely among individuals, with greater risk of intrasurgical bleeding with larger vessels (>2mm) (Maridati et al, 2014), in severely atrophic ridges and at the area of the first upper molar, where the distance between AAA and the alveolar crest is shorter (Rodella et al, 2010; Valente, 2015).

The upper limit of the antrostomy is directly related to the length of the implant to insert (Wallace et al, 2012; Rahpeyma et al, 2015) 15mm from the bony crest is considered a safe distance to prevent vascular damage (Rodella et al, 2010; Kang et al, 2013; Bernardi et al, 2015). However, in a variable proportion of MS, AAA is located closer to the ridge (Kang et al, 2013), which increases the chances of haemorrhagic complications, particularly for patients whose AAA diameter ranges from 1 to 2mm where the risk for bleeding could reach 57% (Ella et al, 2008). Despite this fact, there are currently no studies that focus on identifying factors explaining AAA course variations at the anterolateral sinus wall invading the aforementioned safe-distance. Thus, the aim of this investigation was to identify and model the variables related to patients at risk of iatrogenic bleeding during SLS whose AAAs are located within 15mm of the bony crest.

### 3.3.3. Methods and materials

In order to achieve the aims of this investigation, a retrospective observational study was designed that met the requirements of the university's Ethics Committee. Having obtained informed consent, the study was carried out from March to November 2015 at the Radiology Unit of the School of Medicine and Dentistry of the University of Santiago de Compostela (Spain).

CBCT explorations were identified using the unit's database, and retrieved if they fulfilled the inclusion criteria, namely explorations performed for implant-treatment planning in maxillary edentulous or subsinusally edentulous patients, or subjects with (an) upper first molar(s) missing. Exclusion criteria were: poor image quality, sinus disorders or previous history of sinus surgery or grafting. As a result, 240 MS with clearly defined AAA were selected out of 466 sinuses that met the inclusion criteria.

All patients were explored by means of a cone beam CT (I-CAT, 17-19. Imaging Sciences International, 1910 North Penn Toad, Hatfield, USA) with its I-CAT software (Imaging Sciences International) set at a resolution of 0.3 voxels with 8.9 seconds of capture time. According to previous findings (Rodella et al, 2012; Valente, 2015), the course of AAA lies closer to the bony crest at the upper first molar level, so this location was selected for performing the coronal sections used in this study.

Two researchers (ML & AG) used the resources provided by the proprietary software (I-CATvision) to undertake linear measurements in CBCT explorations.

The relative uncertainty (standard deviation of the measurement divided by its mean and expressed as a percentage from 0% to 100%) was chosen for determining the observational errors. The variables considered (with its relative uncertainty) included: distance from AAA to sinus floor (0%), and distance from AAA to alveolar crest (0%). The outcome variable was “distance of AAA from the bony crest”, considered both as continuous and dichotomous (coded as “1” for distances  $\leq 15$ mm -risk for iatrogenic damage- and “0” for higher values).

Additional potentially related co-variates, such as gender, pattern of edentulism (maxillary edentulous, subsinusally edentulous, or upper first molar missing), and

course of the artery (fully intraosseous; intrasinusal -between the Schneiderian membrane and the sinus bony wall-; or superficial -on the outer cortex of the lateral sinus wall) were also studied. The residual ridge was categorised according to Cawood & Howell (1988) as class II: immediately post extraction; class III: well-rounded ridge; class IV: knife-edge ridge; class V: flat ridge; and class VI: depressed ridge form. Other variables considered in this investigation were: thickness of the lateral sinus wall, height of the residual bony crest, width of the residual alveolar ridge (at the basal and crestal levels) and width of the MS.

### **Statistical analysis**

The study unit for this research was not the patient, but the MS. Descriptive statistics are summarised using frequencies for categorical variables and the median and mean (central trend statistics), together with the inter-quartile range (IQR) as spread indicant for the quantitative ones.

In order to model the chances of AAA detection, the generalized additive models (GAM) approach (Wood, 2011) was chosen, as it permits modelling the effect of co-variants in a flexible manner. The best multivariate model is automatically selected.

All analyses were undertaken using the R software (R Core Team, 2015) with the mgv package for GAM modelling.

### **3.3.4. Results**

A total of 240 MS were studied (111 males, 46.25%, and 129 females, 53.75%). The median age of the participants was 58 years (IQR: 52-66). The median width of the sinus lateral bony wall was 11.5mm (IQR: 9.5-4.1), and the AAA mostly followed a fully intraosseous course within it (n=117; 48.7%) with diameters >1mm in most cases (80.5%).

The main subsinusal bone resorption patterns were the well-rounded (class III:106; 44.17%) and flat ridge (class V: 52; 21.63%) types, with less frequent presentations of class II: 21 (8.75%); class IV: 30 (12.5%); and class VI: 31 (12.9%). The median ridge height was 7.40mm (IQR: 5.27-9.85) (Table 7).

Table 7. Main features of the sample studied (n=240)

Variables	n	(%)
<b>Gender</b>		
Male	111	46.25
Female	129	53.75
<b>AAA position</b>		
Fully intraosseous	117	48.75
Superficial	8	3.33
Intrasinusal	115	47.91
<b>AAA diameter</b>		
≤ 1 mm	47	19.58
>1 ≤ 2mm	162	67.50
>2 mm	31	12.91
<b>Pattern of edentulousness</b>		
Fully edentulous maxilla	32	13.34%
Subsinusal edentulousness	173	72.08%
Upper first molar missing	35	14.58%
	<b>Mean</b>	<b>Median (IQR)</b>
<b>Age (years)</b>	58.39	58 (52-66)
<b>Diameter of AAA</b>	1.35	1.30 (1.00-1.60)
<b>Distance from AAA to sinus floor (mm)</b>	7.66	7.10 (5.20-9.70)
<b>Distance from AAA to alveolar crest (mm)</b>	15.26	14.90 (12.20-17.50)
<b>Maxillary sinus width (mm)</b>	11.7	11.5 (9.50-14.10)
<b>Thickness of the lateral sinus wall (mm)</b>	2.53	2.0 (1.50-2.70)
<b>Height of the residual alveolar ridge (mm)</b>	7.76	7.40 (5.27-9.85)
<b>Width of the residual alveolar ridge (basal level) (mm)</b>	10.18	10.15 (8.30-12.12)
<b>Width of the residual alveolar ridge (crestal level) (mm)</b>	6.68	6.30 (4.60-8.65)

Univariate models have shown a relationship between the AAA-alveolar crest distance and the pattern of edentulousness, bone resorption, height of the residual ridge, distance of AAA to the sinus floor, sinusal area under the artery, and the width of the MS. The chances for an AAA-alveolar crest distance  $\leq 15$ mm increase in wider sinuses with lower, subsinusally edentulous crests (Table 8).

**Table 8.** Univariate GAM logistic models for AAA distance to the bony crest ( $\leq 15\text{mm}$  vs  $> 15\text{mm}$ )

Univariate GAM logistic models	Estimate (B)	Standard Error	Z value	p-value	Degrees of freedom (df)	Model's Chi Square	Model's p-value
<b>Gender</b>					1	0.52	0.46
Intercept	0.23	0.19	1.23	0.21			
Female	-0.18	0.25	-0.76	0.46			
<b>Position of AAA</b>					2	3.93	0.14
intercept	-1.94	1.06	-1.82	0.06			
Fully intraosseous	2.13	1.08	1.96	0.04*			
Intrasinusal	2.13	1.08	1.96	0.04*			
<b>AAA diameter</b>					2	0.56	0.75
Intercept	0.04	0.29	0.14	0.88			
Diameter (1-2mm)	0.15	0.33	0.46	0.63			
Diameter (> 2 mm)	-0.10	0.46	-0.23	0.81			
<b>Pattern of edentulousness</b> (referencia : upper first molar missing)					2	8.01	0.01*
Intercept	1.06	0.38	2.74	0.00			
Fully edentulous maxilla	-1.44	0.52	-2.72	0.00*			
Subsinusal edentulousness	-1.00	0.41	-2.41	0.01*			
<b>Classification of posterior maxilla</b> (Referencia: depressed ridge form)					4	26.48	2.53e-0.5*
Intercept	1.05	0.41	2.57	0.01			
Class IV (Knife-edge ridge)	-0.78	0.55	-1.42	0.15			
Class V ( Flat ridge)	0.04	0.52	0.08	0.93			
Class II (post-extraction)	-2.21	0.65	-3.38	0.000*			
Class III (well-rounded ridge)	-1.39	0.45	-3.07	0.002*			
<b>Univariate GAM logistic models</b>				<b>Explained deviance (%)</b>	<b>Effective degrees of freedom (edf)</b>	<b>Model's Chi square</b>	<b>Model's p-value</b>
<b>Age (years)</b>					2.23	6.30	0.09
<b>Thickness of the lateral sinus wall (mm)</b>					1.64	1.84	0.39
<b>Height of the residual alveolar ridge (mm)</b>				20.3	2.10	40.37	1.20e-08*
<b>Distance from AAA to sinus floor</b>				19.6	2.28	35.83	6.58e-08*
<b>Width of the residual alveolar ridge (basal level) (mm)</b>					2.84	8.00	0.09
<b>Width of the residual alveolar ridge (crestal level) (mm)</b>					1.00	2.01	0.15
<b>Maxillary sinus width (mm)</b>				2	1.00	6.02	0.01*
<b>AAA diameter</b>					1.00	1.32	0.24
<b>Area sinusal bajo la arteria</b>				7	2.19	12.62	0.004*

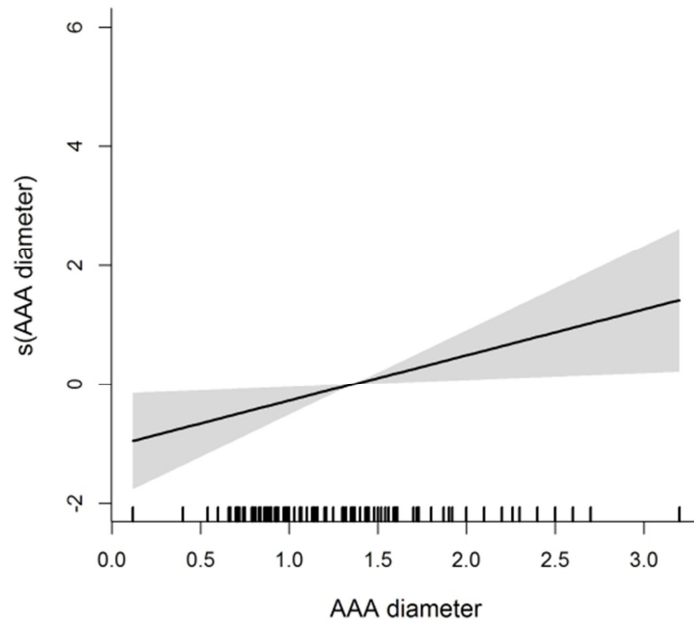
Yet, when distance is considered as a continuous variable, the best multivariate model showed an explained deviance of 67% and included AAA diameter, distance AAA-sinus floor, sinus width, and shape, height and width of the residual ridge. ( $Y = \alpha + \beta_1 \text{ ridge shape} + f_1 (\text{distance from AAA to sinus floor}) + f_2 (\text{diameter of AAA}) + f_3 (\text{width of the residual alveolar ridge –basal level-}) + f_4 (\text{width of the residual alveolar ridge –crestal level-}) + f_5 (\text{MS width})$ , where  $f_1$  to  $f_5$  represent smooth functions of covariates (Table 9).

**Table 9.** Multivariate model

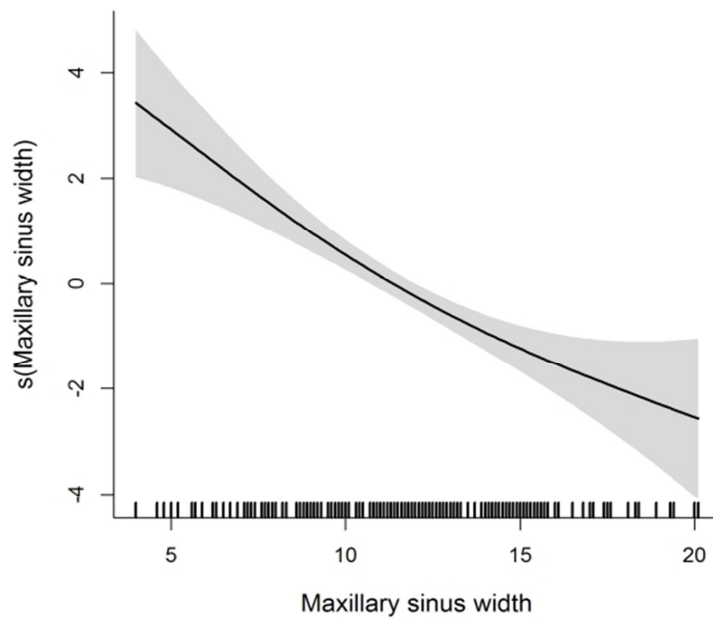
Multivariate		Percentage of deviance explained by the model = 67%						
Parametric part of the model	Estimate ( $\beta$ )	Std. Error	Z value	p-value	Effective degrees of freedom (edf)	Degrees of freedom (df)	F (Chi square)	Model's p-value
<b>Classification of posterior maxilla</b> (Reference: depressed ridge form)								
Intercept	12.43	0.53	23.14	<2e-16*		4	19.8	5.3e-16*
Class IV (Knife-edge ridge)	2.57	0.76	3.36	0.000*				
Class V (Flat ridge)	1.24	0.66	1.88	0.06				
Class II (post-extraction)	3.07	0.84	3.64	0.000*				
Class III (well-rounded ridge)	4.44	0.61	7.2	8.4e-12*				
<b>Flexible part of the model</b> (smooth terms)					Effective degrees of freedom (edf)	Degrees of freedom (df)	F (Chi square)	Model's p-value
<b>AAA diameter</b>					1.00		4.03	0.04*
<b>Distance from AAA to sinus floor</b>					1.00		299.66	<2e-16*
<b>Maxillary sinus width</b>					1.72		18.08	2.65e-08*
<b>Width of the residual alveolar ridge (basal level)</b>					1.54		7.73	0.000*

The diameter of AAA is significant in the multivariate model, as larger AAAs are found further from the crest whereas thinner AAAs are closer to the crest (within the  $\leq 15$ mm safe distance). AAA is also closer to the ridge when the distance AAA-floor of

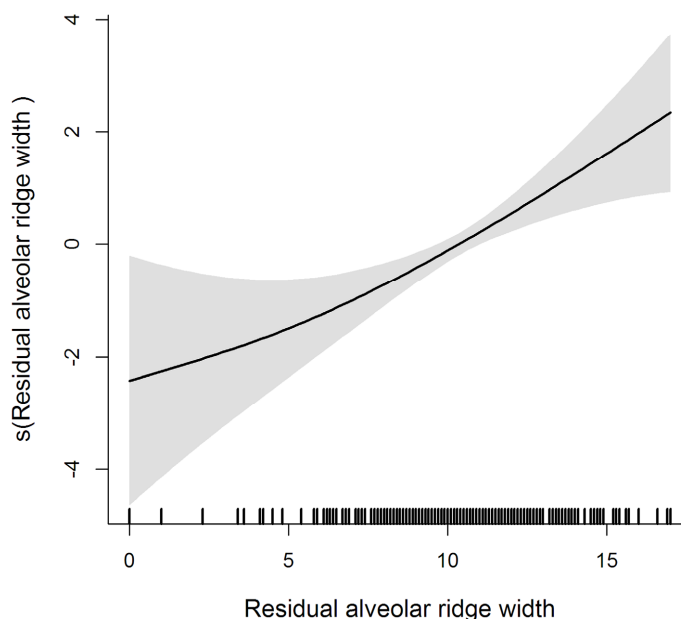
the sinus is short and the sinus is wide. Contrarily, ridges with less resorption and therefore wider at the basal and crestal levels, show significant association to a higher course of the vessel (Figures 10-12).



**Figure 10.** Flexible effect of AAA diameter on the distance to the alveolar crest



**Figure 11.** Flexible effect of maxillary sinus width on AAA distance to the alveolar crest



**Figure 12.** Flexible effect of width of the residual alveolar ridge on AAA distance to the alveolar crest

### 3.3.5. Discussion

There have been reports of massive bleeding due to accidental vascular damage during SLS by lateral (Chan & Wang, 2011) or even transcresal approaches (Jensen et al, 2012). Bleeding results in longer operative times and favours further complications such as perforation of the sinus membrane, or reduction of blood supply and displacement of the graft (Maridati et al, 2014). Certain anatomic features, such as the diameter and position of the AAA together with its proximity to the alveolar crest, may increase the likelihood of these kind of complications (Varela-Centelles et al, 2015; Valente, 2015). Arteries with a diameter below 1mm are not a problem (Mardinguer et al, 2007), but those larger than 2mm may represent a risk for bleeding (Maridati et al, 2014). In current literature the AAA is reported to present an average diameter ranging from 0.9mm to 15mm (Ilgüy et al, 2013). Our findings are consistent with previous reports, with values around 1.3mm and >1mm in 80% of the sinuses.

The position of the vessel regarding the lateral wall of the sinus also has a bearing on the surgery with a greater risk of haemorrhage. Therefore, for intrasinusal

AAAs located between the sinus membrane and the bony wall, the process of membrane detachment is more critical (Kang et al, 2013). This situation has been reported as the second most common (Varela-Centelles et al, 2015; Valente, 2015) and accounts for 47.9% in our series. When the vessel follows a superficial course, external to the lateral wall of the sinus, the risk for haemorrhage would be higher when making incisions, not only during antrostomy (Rodella et al, 2010). This location does not reach 8% in any case series (Güncü et al, 2011; Jung et al, 2011; Kang et al, 2013; Ilgüy et al, 2013). Previous reports acknowledge AAA mostly follows a fully intraosseous course in the sinus lateral bony wall (Kang et al, 2013; Ilgüy et al, 2013; Güncü et al, 2012), which occurred in 48.7% of the sinuses in our study.

The location of AAA in relation to the alveolar ridge also influences osteotomy, with reported average distances ranging from 11.2mm (Yang & Kye, 2014) to 18.3mm (Rosano et al, 2011). The variations in extreme values are wider -2.8 mm to 31.7mm- (9.20), most likely due to variation in the height of the residual ridge and in the distance AAA-floor of the MS. Our results show a mean value of 15.2mm for an average AAA-sinus floor distance of 7.6mm. Despite a moderate (20-31%) proportion of cases where AAA invades the safe distance of  $\leq 15$ mm (9.23), our data revealed this phenomenon occurs in up to 48.6% of cases and therefore it should always be taken into account when undertaking SLS procedures.

This investigation has permitted the identification of risk profiles where patients with depressed ridges and sagittally wider sinuses have higher chances for a course of AAA invading the safety distance reported in the literature. On the other hand, patients with rounded and wide alveolar crests whose AAA are identified at distances greater than 6mm from the sinus floor would be at lower risk for bleeding complications. Moreover, larger arteries tend to locate farther from bony crest with less probability for iatrogenic damage.

### **Surgical recommendations**

Surgical planning based upon clinical records and CBCT explorations with the use of piezoelectric devices for osteotomy permits a reduction of the surgical risk (Valente, 2015). Some authors have suggested ligating arteries  $>3$ mm to prevent severe

iatrogenesis (Rosano et al, 2001; Jung et al, 2011). Alternative specific techniques (double window) may also be used to avoid the AAA during antrostomy and to reduce the risk of bleeding (Varela-Centelles et al, 2015; Valente, 2015). In situations where AAA follows a mainly intrasinus course, the process of detachment and elevation of the Schneiderian membrane should be particularly careful. When the course of the vessel is fully extraosseous, the risk for bleeding accidents is related to the incision and flap design.

### **3.3.6. Conclusions**

Bearing in mind the inclusion criteria and the limitations of this investigation, it is concluded that there is a high proportion of MS where AAA follows a course close to the alveolar crest ( $\leq 15\text{mm}$ ), which was classically considered a safe distance for SLS. This position is related to the presence of an atrophic crest (depressed ridge form) and wide MS where the distance of the vessel to the floor of the sinus is small. This information may permit a better surgical planning of SLS procedures.

## **3.4. CHAPTER IV: Diameter of alveolar antral artery in the lateral sinus wall. A study of related factors.**

### **3.4.1. Abstract**

This study was undertaken with the aim of identifying variables related to the diameter of AAA in the lateral sinus wall. A sample of 240 MS were studied at the first upper molar area. The main outcome chosen was the diameter of the vessel and the covariates investigated were gender, pattern of tooth loss, type of residual crest, thickness of the lateral sinus wall, height of the residual ridge, width of the ridge, and sinus width. The modelling of the probability for AAA diameter was undertaken using logistic generalized additive models (GAM).

It is concluded that arteries with a course that lies away from the bony crest, in subsinusally edentulous male patients whose sinus is about 14mm wide and their lateral

wall is 4mm thick, are likely to be larger, and would therefore require careful and detailed surgical planning.

**Key words:** cone-beam computed tomography, blood vessels, sinus floor augmentation, intraoperative complications.

#### 3.4.2. Introduction

The AAA is an anastomosis of the PSAA and the IOA, which runs through the anterolateral wall of the MS to ensure blood supply to the wall itself, the periosteum, and the sinus membrane (Valente, 2015; Varela-Centelles et al, 2015). A variety of surgical procedures, such as the Le fort I osteotomy or Caldwell-Luc surgery, as well as maxillary fractures may affect AAA (Rahpeyma et al, 2015). During SLS procedures, a germane bleeding may displace the flap and compromise its integration (Maridati et al, 2014).

Despite identifying profiles at risk for bleeding complications (larger AAA) would be useful in a number of circumstances, no reports on this topic could be retrieved. Therefore, the aim of this study was to identify variables related to the diameter of AAA in the lateral sinus wall.

#### 3.4.3. Methods and materials

This study is a secondary analysis of a sub-sample of 240 MS selected from a total 466 sinuses explored for surgical planning of implant-supported prosthesis in the subsinusal area within a retrospective observational study undertaken at the Radiology Unit of the School of Medicine and Dentistry of the University of Santiago de Compostela (Spain) after obtaining approval by the university Ethics Committee.

Patients were explored with a cone beam CT (I-CAT, 17-19. Imaging Sciences International, 1910 North Penn Toad, Hatfield, USA) using I-CAT software (Imaging Sciences International). The coronal sections used in this investigation were obtained at

the first upper molar area, given the vicinity of the AAA to the alveolar ridge (Valente, 2015). The main outcome was the diameter of the vessel and the co-variables investigated were gender, pattern of tooth loss, type of residual crest (Cawood & Howell, 1988), thickness of the lateral sinus wall, height of the residual ridge, width of the ridge, and sinus width.

### **Statistical analysis**

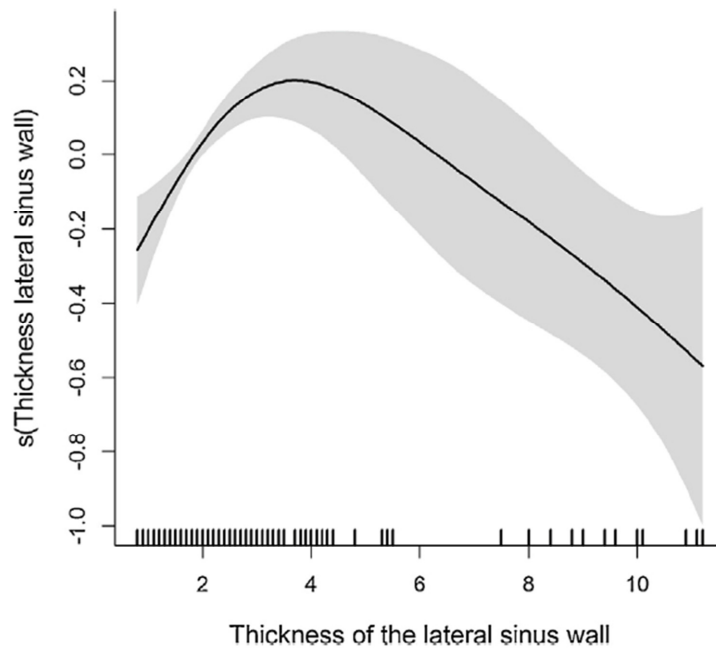
The MS was considered as the study unit. The modelling of the probability of AAA diameter was undertaken using logistic generalized additive models (GAM) using the R software (The R Foundation, Vienna, Austria.) and the mgcv package for GAM modelling.

#### **3.4.4. Results**

The sample of 240 MS (males 46.25 %) had a median age of 58 years (IQR: 52-66). The median of the diameter of the vessel was 1.30mm (IQR= 1.00 -1.60). AAA mainly described an intraosseous course (n=117; 48.75%) with gauges ranging between 1 and 2mm (n=162; 67.50%).

The best multivariate model was found to be:  $Y = \alpha + \beta_1 \text{ gender} + \beta_2 \text{ (pattern of tooth loss)} + f_1 \text{ (thickness of the lateral sinus wall)} + f_3 \text{ (sinusal area under the artery)} + f_4 \text{ (distance from AAA to alveolar crest)}$ , where Y= artery diameter. This model explains a deviance of 32%. Males showed significantly larger vessels than women.

When considered as continuous variables, both the distance AAA-bony crest and the thickness of the lateral sinus wall have proven a major effect on the artery gauge. This effect for a large vessel increases with the distance from the crest. The same phenomenon occurs when the thickness of the lateral wall is up to 4mm. Beyond this value, the effect decreases (Figure 13).



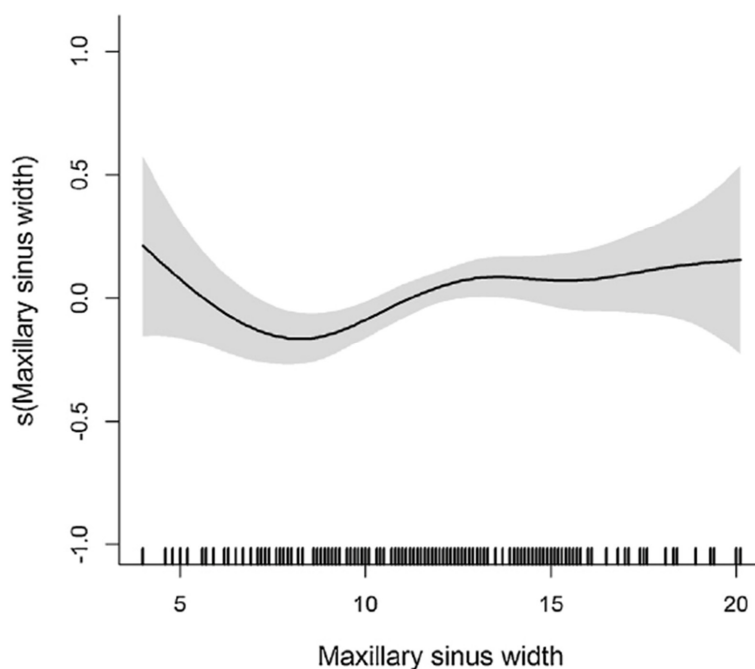
**Figure 13.** Thickness of the lateral sinus wall.

Our data has also shown that the wider the MS, the higher the chances of finding a large AAA, although this effect is only true for narrow sinuses (7-14mm) (Figure 14, Table 10).



**Table 10.** Multivariate model. Factors associated to AAA diameter

Multivariate		Percentage of deviance explained by the model = 32%						
Parametric part of the model	Estimate (β)	Std. Error	Z value	p-value	Effective degrees of freedom (edf)	Degrees of freedom (df)	F (Chi square)	Model's p-value
Intercept	1.53	0.07	19.40	<2e-16 *		1	14.24	0.000*
<b>Gender</b>								
Female	-0.19	0.05	-3.56	0.000 *				
<b>Pattern of edentulousness</b>						2	3.42	0.03
Fully edentulous maxilla vs upper first molar missing	0.07	0.10	0.74	0.45				
Subsinusal edentulousness vs upper first molar missing	-0.11	0.07	-1.51	0.13				
Subsinusal edentulousness vs fully edentulous maxilla	-0.18	0.07	-2.36	0.01*				
Flexible part of the model (smooth terms)					Effective degrees of freedom (edf)	Degrees of freedom (df)	F (Chi square)	Model's p-value
Thickness of the lateral sinus wall					3.16		7.61	1.99e-05*
Distance from AAA to sinus floor					1.00		7.41	0.006*
Maxillary sinus width					3.84		2.51	0.04*
Sinus area under the artery					3.66		2.79	0.03*



**Figure 14.** Maxillary sinus width

### 3.4.5. Discussion

There is a wide variation in AAA diameter (Maridati et al, 2014) and during SLS, the risk for per-operative bleeding for vessel diameters between 1-2mm is about 57%, (Cawood & Howell, 1988) and greater still for arteries >2mm.

The variables patient, gender and thickness of the sinus wall have been independently related to AAA gauge in previous reports (Kim et al, 2011; Kang et al, 2013). Our study permitted the synthesis of this relationship in a multivariate model. Moreover, the use of flexible models allowed us to demonstrate that the association with the thickness of the sinus wall only occurs for values up to 4mm, and also that the maxillary sinus width is related to AAA diameter for values between 7 and 14mm.

Bearing in mind the limitations of these kind of studies, it is concluded that arteries which follow a course that lies away from the bony crest, in subsinusally edentulous male patients whose sinus is about 14mm wide and their lateral wall is 4mm thick, are likely to be larger and therefore would require careful and detailed surgical planning.





## 4. SPANISH ABSTRACT

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## 4. SPANISH ABSTRACT

La vascularización del seno maxilar (SM) es un condicionante mayor en las cirugías regenerativas de elevación sinusal complementaria a la inserción de implantes dentales. En este sentido, el estudio preoperatorio mediante tomografía computarizada (CT) y tomografía computarizada de haz cónico (CBCT), podría contribuir a la identificación de los vasos que discurren por la pared lateral del SM y a la planificación quirúrgica de la osteotomía. Sin embargo, no existen datos concluyentes sobre el rendimiento diagnóstico del CT/CBCT en la detección de estas estructuras, ni se conocen los condicionantes que van a permitir la identificación de la arteria alveolar antral (AAA) mediante este procedimiento radiológico.

En base a estas circunstancias los objetivos de este trabajo de Tesis han sido el realizar un meta-análisis para obtener información sistematizada sobre la prevalencia de la arteria alveolar postero superior (AAPS) en la pared lateral del SM usando tecnología CT/CBCT en pacientes candidatos a la elevación de seno maxilar (ESM) y estudiar las variables asociadas a la detección de la AAA controlando los potenciales factores de confusión y elaborar modelos explicativos que ayuden en la planificación prequirúrgica de estos pacientes.

### **4.1. Detección de la AAPS en la pared lateral del SM usando CT/CBCT. Revisión sistemática y metaanálisis de la prevalencia.**

La perforación de la membrana sinusal constituye la complicación más frecuente de la ESM, 19.5% (0% al 58.3%) de todas las elevaciones sinusales. Tras ella, el sangrado profuso constituye la segunda complicación intraoperatoria, que ocurre cuando se efectúa la antrostomía con material rotatorio. La lesión vascular accidental durante ESM puede causar una hemorragia masiva, por lo que la planificación prequirúrgica y la identificación de los vasos sanguíneos cobra una especial relevancia. En este sentido, la

anastomosis intraósea entre la AAPS y la arteria infraorbitaria (AIO) puede ser una zona con mayor riesgo de que ocurran complicaciones hemorrágicas durante la cirugía de ESM. La rama intraósea de la AAPS en la pared sinusal adopta comúnmente un trayecto recto o curvo, cuyo punto más próximo a la cresta ósea, es a nivel del primer molar. Esta anastomosis proporciona irrigación a la membrana de Schneider, y también contribuye a la integración del injerto y a la cicatrización de la herida quirúrgica.

Se estima que durante la antrostomía en el procedimiento ESM, el corte accidental de los vasos intraóseos en la pared lateral, podría causar hasta un 20% de hemorragias significativas, aunque en series de casos clínicos, las hemorragias perioperatorias se han presentado en una menor proporción. También, se han descrito de forma esporádica, hemorragias postoperatorias severas en ESM usando la vía transcrestal.

Se han encontrado arterias intraóseas hasta en un 83% de los senos analizados al utilizar material cadavérico edéntulo como modelo experimental, durante la osteotomía de la pared sinusal en áreas del primer y segundo molar en la ESM. Por ello, la identificación de las estructuras vasculares previamente a la ESM es fundamental para evitar complicaciones quirúrgicas innecesarias.

A pesar que diferentes estudios anatómicos han identificado de forma consistente la anastomosis intraósea de la AAPS en el 100% de los SM; un artículo de revisión de la evidencia al respecto ha sugerido que la CT no debería usarse para la localización de estas estructuras en base a la escasa prevalencia de arterias intraóseas detectadas mediante este tipo de radiodiagnóstico. Sin embargo, desde entonces diversos estudios radiológicos utilizando CT y CBCT han incrementado la capacidad de detección de la AAPS en la pared sinusal por lo que este tema debería ser reanalizado. Estas circunstancias son las que justifican la necesidad de una revisión sistemática sobre la capacidad de detección de la AAPS en la pared lateral del seno mediante CT/CBCT.

Para ello se llevó a cabo una revisión sistemática usando las siguientes bases de datos: Medline, Embase y Proceedings Web of Science. La estrategia de búsqueda fue: (“blood supply” OR “maxillary arterial” OR “arterial supply” OR “vascular”) AND (“maxillary sinus” OR “sinus floor elevation” OR “sinus lift” OR “sinus augmentation”), tanto en medical subject headings (MeSH), como en texto libre. Los estudios fueron incluidos en caso de cumplir los siguientes criterios de elegibilidad:

- I) Estudios que proporcionan datos de prevalencia en la detección de anastomosis de la AAPS en la pared lateral del seno maxilar mediante CT y/o CBCT.
- II) Estudios cuya muestra está constituida exclusivamente por pacientes con tramos edéntulos en el área subsinusal del maxilar.
- III) Sin restricción idiomática.

Como criterios de exclusión se consideraron: estudios postmortem, o estudios con muestras mixtas (vivos y material cadavérico) que no proporcionan datos de forma independiente. Para la evaluación de la calidad se ha utilizado la guía STROBE para estudios observacionales.

Para llevar a cabo el análisis y síntesis de datos se computó la prevalencia de la AAPS en la pared lateral del SM para cada estudio. Para ello se dividieron el número de senos en los cuales se detecta la arteria por el número total de senos examinados. Para calcular el 95% de intervalos de confianza (95%CI) se utilizó el método exacto de Newcombe y Altman. También se midió el peso estimado de los estudios de prevalencia por la inversa de su varianza para computar la prevalencia conjunta y su intervalo de confianza. Se calcularon los efectos fijos y aleatorios totales estimados. Respecto a la heterogeneidad, se consideró el modelo de efectos aleatorios ya que proporciona resultados más fiables. Todos los análisis se llevaron a cabo con el software HEpiMA<sup>®</sup> version 2.1.3 .

Tan solo 10 estudios transversales, publicados en esta última década, cumplieron los criterios de elegibilidad. Estos estudios agrupan un total de 1939 pacientes y 2174 senos maxilares (la unidad de estudio). 6 estudios han utilizado CT para identificar la

anastomosis intraósea de la AAPS, mientras otros 4 utilizaron tecnología CBCT con la misma intención. Los estudios radiográficos incluidos en el meta-análisis han mostrado una prevalencia total de AAPS en la pared lateral del seno del 64,9% (95%CI=50,5-79,2). Los estudios CBCT han mostrado una mayor detección de AAPS, con una prevalencia total del 78,1% (95%CI=50,5-79,2), y un rango que va desde 52,8% hasta el 94,4%, mientras los estudios con CT detectan la AAPS en una menor proporción, mostrando una prevalencia total del 54.4% (95%CI=48.4-60.3). Los estudios radiográficos llevados a cabo mediante CT informan de un calibre medio de la arteria mayor que los encontrados en estudios con CBCT. Además, más el 60% de los SM analizados con CBCT presentan <1mm de calibre de la AAPS, mientras que esta proporción es menor en senos estudiados mediante CT.

También se ha descrito un amplio rango de distancias medias desde la arteria AAPS hasta la cresta ósea maxilar, que va desde 11,2 hasta 18mm. Por otra parte, tan solo 4 estudios informan sobre la posición medio lateral de la AAPS en la pared del SM; en 3 de ellos la arteria adopta mayoritariamente un trayecto completamente intraóseo, mientras en uno de los estudios, la arteria ocupa frecuentemente una posición intrasinusal entre la membrana de Schneider y la pared ósea del SM. En todas las series ha sido descrita la posición superficial con menor frecuencia, con un rango que va desde el 5.2% al 7.7% de los senos estudiados.

Nuestro estudio demostró que la evaluación preoperatoria con CBCT permite detectar la AAPS en una alta proporción de los SM y de forma más efectiva que con el CT tradicional. Debido a de que no existen ensayos clínicos, los datos incluidos en el meta-análisis, proceden de grandes series de casos clínicos con un probable sesgo de selección muestral. Sin embargo, parte de estos estudios deben asumir limitaciones relacionadas con falta de control de factores de confusión, como podrían ser la edad, el sexo, y la etnicidad de la muestra, lo que podría amenazar su validez interna. También la localización intrasinusal de la arteria podría escapar de la detección radiológica, y comportarse como un factor de confusión.

La discrepancia entre la presencia de AAPS en el 100% de los especímenes anatómicos y su menor detección radiológica podría deberse al escaso diámetro de las arterias. Así, el calibre medio de las arterias detectadas mediante CT es marcadamente mayor, lo que parece sugerir que tan solo arterias de mayor diámetro podrían ser

detectadas por este procedimiento. El CBCT ha mostrado una mayor sensibilidad en la detección; además ha sido recomendado como “costo-efectivo” comparado con CT estándar en cirugía maxilofacial.

A pesar de la necesidad de la evaluación prequirúrgica de AAPS en la ESM, la relevancia clínica del daño vascular durante la antrostomía, es variable y dependiente del calibre del vaso; así, la sección de vasos con calibres  $<1\text{mm}$  tienen un escaso impacto quirúrgico; mientras diámetros mayores pueden dificultar la visualización y comprometer el procedimiento. En este sentido, los estudios incluidos en el meta-análisis han encontrado unos diámetros medios que oscilan entre 0.9 y 1.5mm. Se han identificado AAPS de mayor calibre asociadas al sexo masculino y a paredes sinusales gruesas, sin embargo la influencia de la edad en el diámetro vascular es controvertida.

Estas circunstancias hacen que la distancia desde de la AAPS y la cresta ósea condicione el diseño quirúrgico de la antrostomía. A pesar de que los valores promedio se encuentran agrupados, se ha publicado un amplio rango de distancias (2,8 -31,7mm), probablemente debido a variaciones anatómicas y a las diferentes dimensiones de la cresta ósea. También la posición de la AAPS, específicamente las parcialmente intraóseas localizadas en la cara interna de la pared lateral del seno, podrían condicionar la técnica quirúrgica debiendo evitarse la injuria vascular durante el proceso de despegamiento de la membrana. Esta posición intrasinusal de la AAPS ha sido diagnosticada entre el 13% y el 63,8% de los senos analizados.

A pesar de que no se han encontrado diferencias significativas, entre cirugía piezoeléctrica y el material rotatorio convencional para la osteotomía en ESM en términos de visibilidad, de tiempo quirúrgico, de perforación de la membrana o de expectativas del paciente; el empleo de la cirugía piezoeléctrica podría estar especialmente recomendado en senos con anastomosis de AAPS de mayor calibre.

Dentro de las limitaciones inherentes a los potenciales sesgos de los estudios considerados en el meta-análisis, se concluye que la prevalencia en la detección de AAPS en la pared sinusal es mayor utilizando CBCT que CT. Además, son necesarios nuevos estudios comparativos que evalúen la capacidad de identificación prequirúrgica de la PSAA mediante procedimientos radiográficos controlando los sesgos potenciales de confusión.

#### **4.2. Detección de la arteria AAA con CBCT. Estudio de los factores asociados y modelos predictivos.**

La ESM con abordaje lateral constituye un procedimiento predecible y seguro de aumento óseo en el sector maxilar posterior para la inserción de implantes. Sin embargo, diferentes complicaciones potenciales deben ser tenidas en cuenta. Como complicaciones postoperatorias específicas figuran: la congestión sinusal, la movilidad del injerto, la sinusitis aguda, o la formación de quistes. Entre las complicaciones intraoperatorias se han descrito: la perforación de la membrana de Schneider, la hemorragia de la AAA y la obstrucción del complejo osteo-meatal. Así, los sangrados accidentales de diferente intensidad secundarios al daño quirúrgico de la AAA representan la segunda complicación más frecuente. En base a estudios observacionales y a series de casos se considera que este evento podría propiciar hasta un 20% de sangrados clínicamente relevantes, e indirectamente enlentecer o postponer el acto quirúrgico, movilizar y disminuir el aporte sanguíneo al injerto, e incrementar la tasa de perforación de la membrana sinusal.

El CBCT ha demostrado superioridad al CT convencional en la identificación de la AAA. Sin embargo, la no detección de la AAA no excluye su existencia, y podría obedecer a su pequeño diámetro (<0,5mm) o a una posición intrasinusal o superficial de la misma. Nuestro meta-análisis encuentra que la prevalencia total de la AAA detectada por medio de CBCT fue de 78,12, intervalo de confianza al 95% (IC95%): 61,25-94,98, con un rango entre 52,8% y 94,4%. Sin embargo también alertaba sobre la validez interna y sesgos potenciales de los estudios incluidos, asociados básicamente a la falta de control de factores de confusión, como son la edad, el sexo o la etnicidad.

En base a la ausencia de estudios previos sobre detección de la AAA que hayan controlado estos factores de confusión, el objetivo de esta segunda parte de la Tesis fue proporcionar información sobre la prevalencia de detección de la AAA mediante CBCT, estudiar las variables asociadas a la detección controlando los potenciales factores de confusión y elaborar modelos predictivos que ayuden en la planificación prequirúrgica de estos pacientes.

Se diseñó un estudio observacional retrospectivo, utilizando CBCTs procedentes de la Unidad de Radiología de la Facultad de Odontología de la Universidad Santiago de Compostela, bajo los estándares del comité de ética de la universidad. Para la selección de los CBCTs se utilizó un gestor de base de datos. Como criterios de inclusión se consideraron pacientes candidatos a rehabilitación implantosoportada con desdentación maxilar completa, o desdentación del área subsinusal, o pérdidas unitarias del primer molar superior. En tanto, los criterios de exclusión fueron: CBCTs con una calidad de imagen deficiente, senos que mostraban patología, así como SM con tratamientos quirúrgicos previos o senos injertados. Todos los pacientes se estudiaron mediante CBCT (i-CAT, 17-19) Imaging Sciences International, 1910 North Penn Toad, Hatfield PA, USA con el I-Cat software (Imaging Sciences International) resolución de 0,3 voxels con 8,9 segundos de tiempo de captura. La medida de precisión utilizada para cuantificar el error de estas observaciones fue la incertidumbre relativa, que consiste en el cociente entre la desviación estándar de la medida y su media (en porcentaje).

La variable respuesta es  $y = \text{detección} / \text{no detección}$  (*dectart*), y como posibles variables categóricas: sexo, lado del paciente (*ladopac*), tipo de dentición (*tipdent*) con tres niveles: desdentado total, parcialmente desdentado y pequeña brecha edéntula y tipo de cresta edéntula. El tipo de cresta ósea residual fue clasificado en base la clasificación de Cawood & Howell (1988), como: 0: inmediata postexodoncia; 1: redondeada; 2: filo de cuchillo; 3: aplanada; 4: deprimida.

Como variables continuas se consideraron la edad, la distancia cresta-suelo del seno (*crestue*), el ancho basal de la cresta ósea residual (*anchbasa*), ancho coronal de la cresta ósea residual (*anchcor*), anchura sagital del seno (*sasgen*). El SM se consideró como unidad de estudio y se expresaron los resultados de las variables categóricas en términos de frecuencias, en tanto para las variables cuantitativas se usaron la media y la mediana como medidas de tendencia central y la desviación estándar y el rango como medidas de dispersión.

Se llevó a cabo la modelización de la probabilidad de detección de la arteria mediante modelos aditivos generalizados logísticos, los cuales permiten modelizar el efecto de las covariables en la respuesta de forma flexible, dado que la variable

respuesta es binominal. Se han ajustado los modelos univariantes con cada una de las variables independientes. Además, los modelos univariantes para variables continuas incluyen la interacción de la covariable con el sexo, dado que en el análisis exploratorio parecen observarse diferencias en la distribución de los valores de las covariables en función del sexo.

Una vez seleccionado el mejor modelo multivariante se determinó su capacidad para discriminar entre la probabilidad de detección de la arteria vs. no detección mediante curvas ROC.

Las características de la muestra se agrupan en la tabla que aparece a continuación:

**Tabla 1.** Características de la muestra estudiada

Detección AAA	Sexo	Curso AAA	Grosor AAA
No: 226	H: 198	Extrasinusal: 8	g 0 (<1mm): 47
Si. 240	M: 268	Intraosea: 117	g 1 (1-2mm): 162
		Intrasinusal: 115	g 2 (> 2mm): 31
		NA´s: 226	NA´s: 226

(H: hombre; M: mujer; NA´s: Arteria alveolar antral no detectada)

### **Modelización de la detección de la arteria (AAA)**

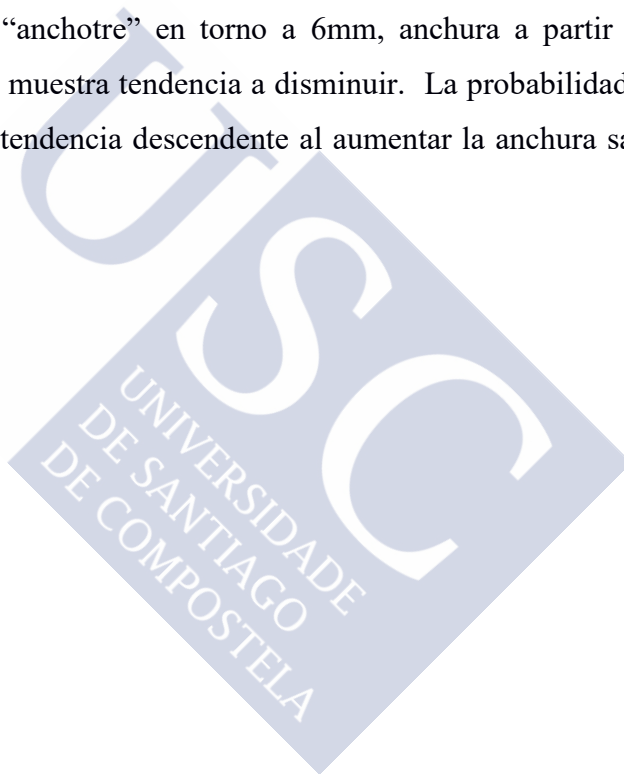
- Modelos univariantes:

Tan solo la variable tipo de cresta tiene efecto significativo, siendo la probabilidad de detección de la arteria significativamente mayor en crestas post-extracción (respecto a las deprimidas) y redondeadas (respecto a crestas deprimidas y aplanadas). Sin embargo, el porcentaje de desviación explicado por dicho modelo es extremadamente bajo.

Por lo que respecta a las variables continuas, tienen efecto significativo en la probabilidad de detección de la arteria las variables “distancia de la cresta al suelo del seno (*crestsue*)”, “ancho coronal de la cresta ósea residual (*anchor*)”, y “anchura sagital

del seno (*sasgen*)”, siendo ésta última la que alcanza un porcentaje explicado mayor, aunque todos ellos en muestran valores muy bajos.

En la Figura 1 se pueden ver los gráficos de la probabilidad de detección de la arteria en función de cada una de las covariables de los modelos univariantes Logit  $\{P(\text{Detección Variable Explicativa})\} = \alpha + f_1(\text{Variable Explicativa})$ . Como se puede ver en el gráfico, la probabilidad de detección de la arteria presenta una tendencia a aumentar al incrementarse la distancia de la cresta al suelo del seno (*crestasue*), si bien el intervalo de confianza es bastante amplio. Respecto a la anchura de la pared del seno (*anchotre*) se puede ver un rápido incremento de la probabilidad de detección de la arteria, hasta valores de “anchotre” en torno a 6mm, anchura a partir de la cual la probabilidad de detección muestra tendencia a disminuir. La probabilidad de detección de la arteria muestra una tendencia descendente al aumentar la anchura sagital de seno (*sasgen*).



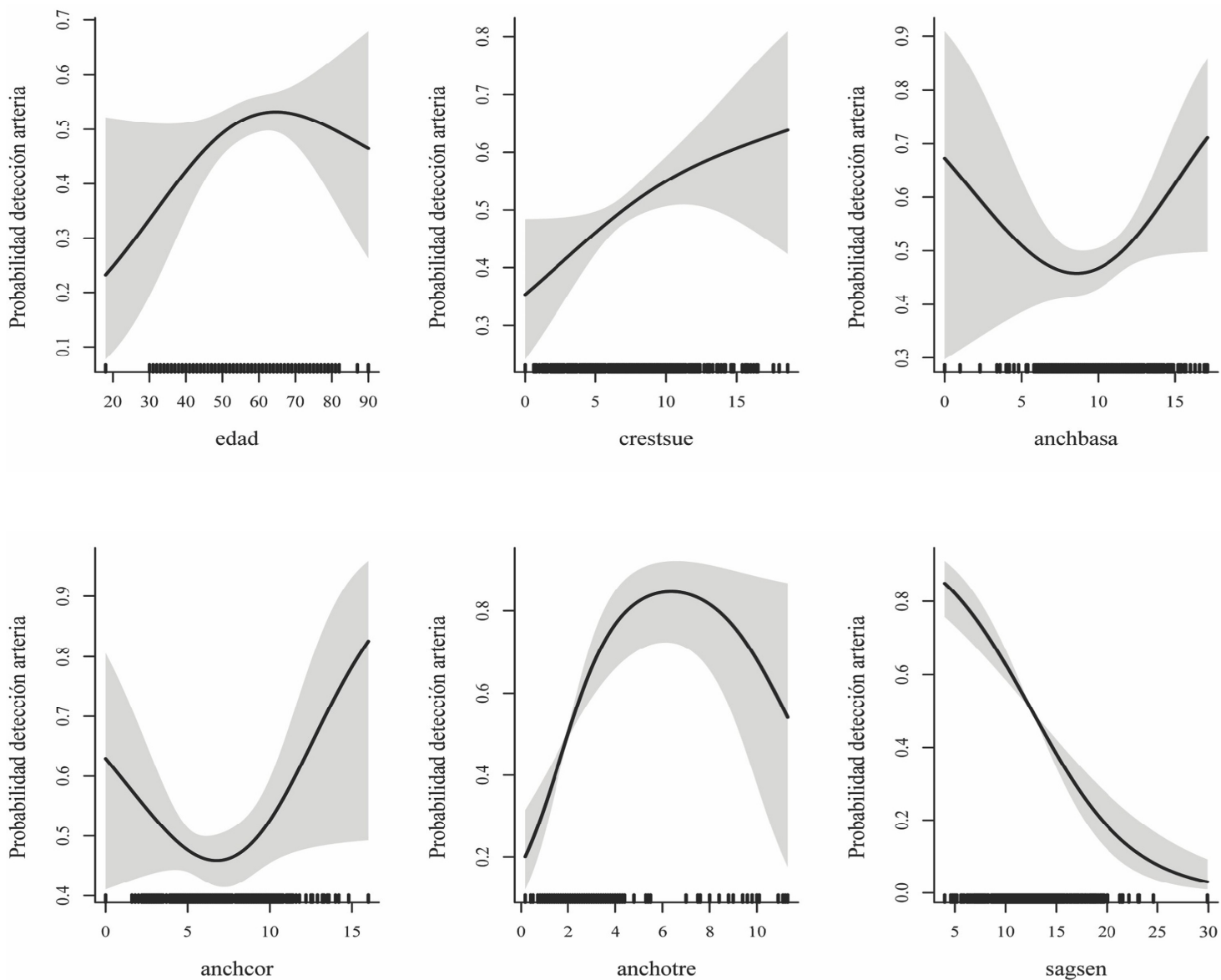


Figura 1. Gráficos de probabilidad de detección de la AAA en relación a cada una de las covariables de los modelos univariantes

### Modelos univariantes con interacción por sexo

Estos modelos se denominan modelos de coeficientes variantes, y son modelos de regresión (flexible) en los que se permite a los coeficientes variar de forma suave como función de otra variable, en este caso el sexo. Tomarían la forma:  $T \text{ Logit } \{P$

$(\text{Detección} | \text{VarExpl}) = \alpha + \text{Sexo Mujer } f_1 (\text{VarExpl}) + \text{Sexo Hombre } f_2 (\text{VarExpl})$ , es decir, que se permite el ajuste de distintas curvas en función del sexo.

Las variables que se relacionan significativamente con la probabilidad de detección de la arteria son: cresta-suelo sólo en las mujeres, y ancho de la pared lateral del seno y anchura sagital del seno en mujeres y hombres. El mayor porcentaje de desviación explicado (aunque muy bajo) lo presenta el modelo que tiene como covariable la anchura de la pared sagital del seno.

En las figuras 2a y 2b se puede ver gráficamente el efecto de cada una de las covariables en la probabilidad de presencia para los hombres y para las mujeres. Como se puede ver, en las mujeres la probabilidad de detección de la arteria aumenta al aumentar la distancia entre la cresta y el suelo, hasta valores de aproximadamente 10mm.

Respecto a la anchura de la pared lateral del seno, la probabilidad es creciente en las mujeres hasta valores en torno a los 6mm, a partir de los cuales empieza a disminuir. En los hombres, sin embargo, la probabilidad es creciente en todo el rango de la variable, si bien el intervalo de confianza es amplio.

En relación a la anchura sagital del seno, la probabilidad es decreciente tanto en hombres como en mujeres al incrementarse dicha anchura, si bien en las mujeres se alcanzan probabilidades superiores (para las anchuras menores) e inferiores (para las mayores) a las alcanzadas por los hombres.

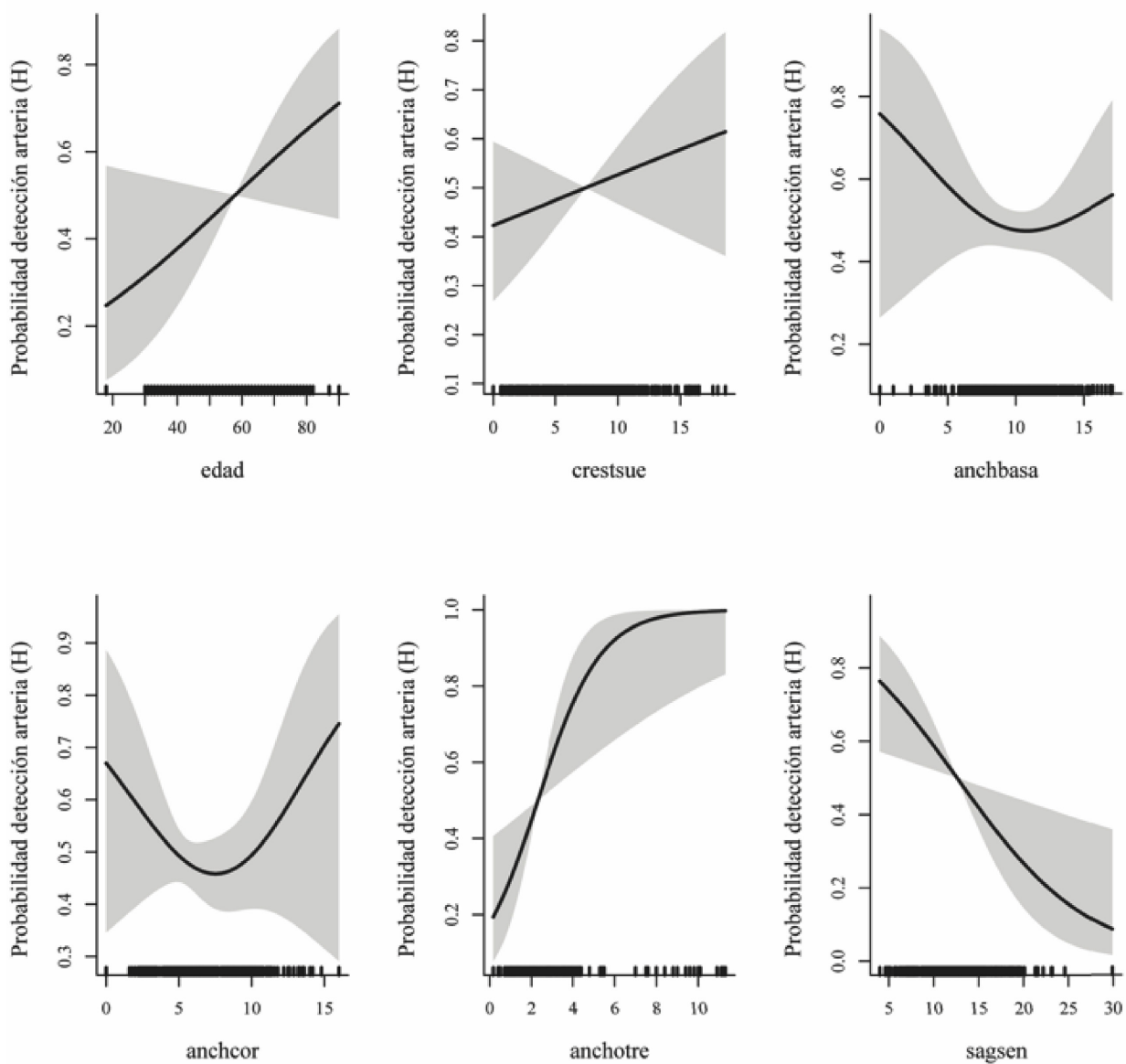
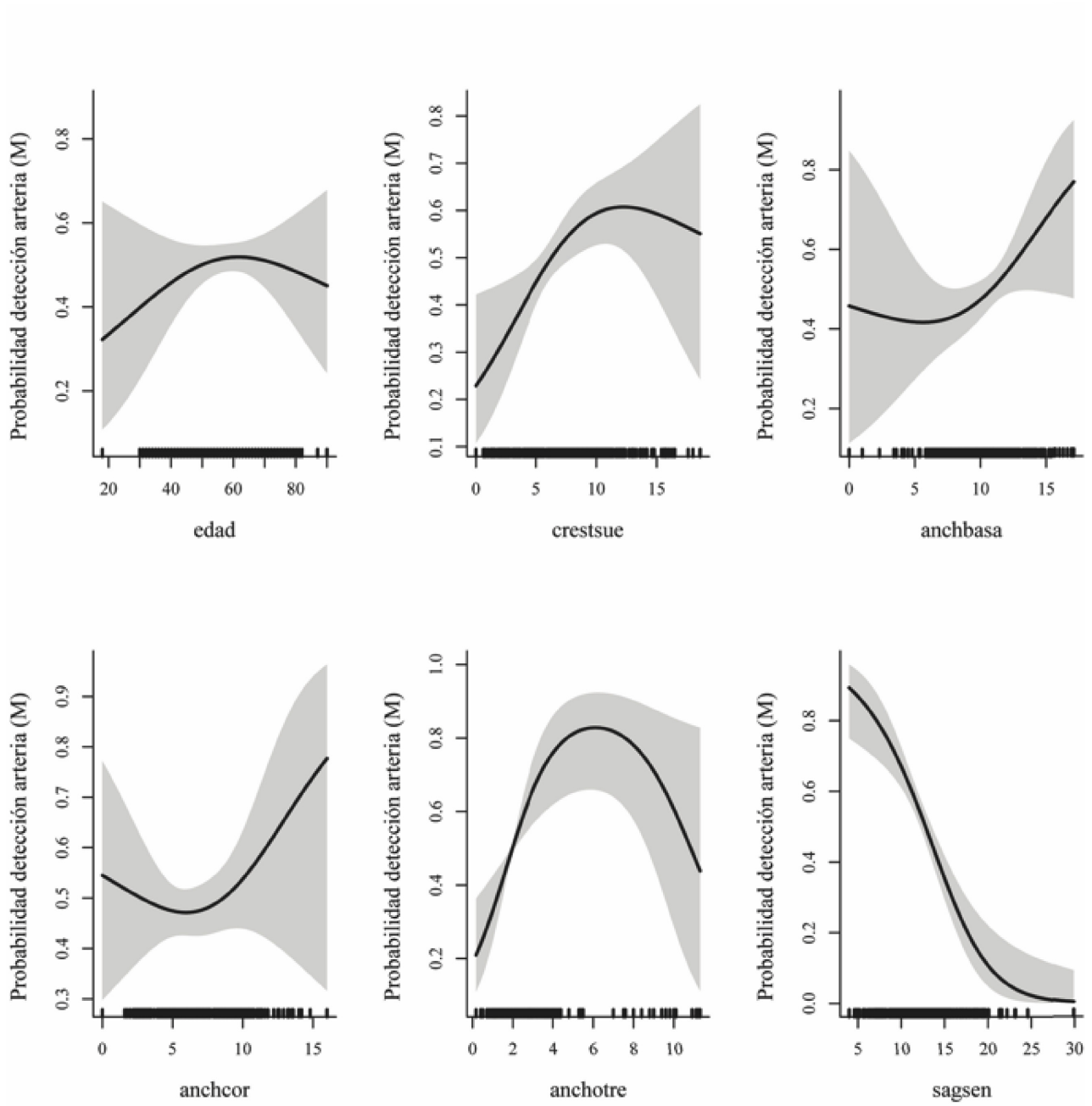


Figura 2a. Probabilidad de detección de la arteria en relación a las covariables de los modelos de interacción por sexo (hombres)



**Figura 2b.** Probabilidad de detección de la arteria en relación a las covariables de los modelos de interacción por sexo (mujeres)

### Modelos multivariantes

El mejor modelo incluye tres variables categóricas (parte paramétrica del modelo) y tres continuas (parte flexible):

Logit  $\{P(\text{Detección}|X_i)\} = \alpha + \beta_1 \text{ Sexo} + \beta_2 \text{ tipo de dentición} + \beta_3 \text{ tipo de cresta}$   
 $f_1$  (distancia cresta-suelo del seno)+  $f_2$  (ancho pared lateral del seno) +  $f_3$  (anchura sinusal). El porcentaje de deviance explicada por dicho modelo es del 21 %.

#### -Modelo multivariante para las mujeres

El mejor modelo multivariante considerando solo a las mujeres, es:

Logit  $\{P(\text{Detección } X_i)\} = \alpha + \beta_1 \text{ tipdent} + \beta_2 \text{ tipocres} + f_1$  (*anchbasa*) +  $f_2$  (*crestsue*) +  $f_3$  (*anchotre*) +  $f_4$  (*sagsen*). El porcentaje de desviación explicado por el modelo es de 31,2%.

Los resultados de la parte paramétrica y de la parte flexible son los siguientes:

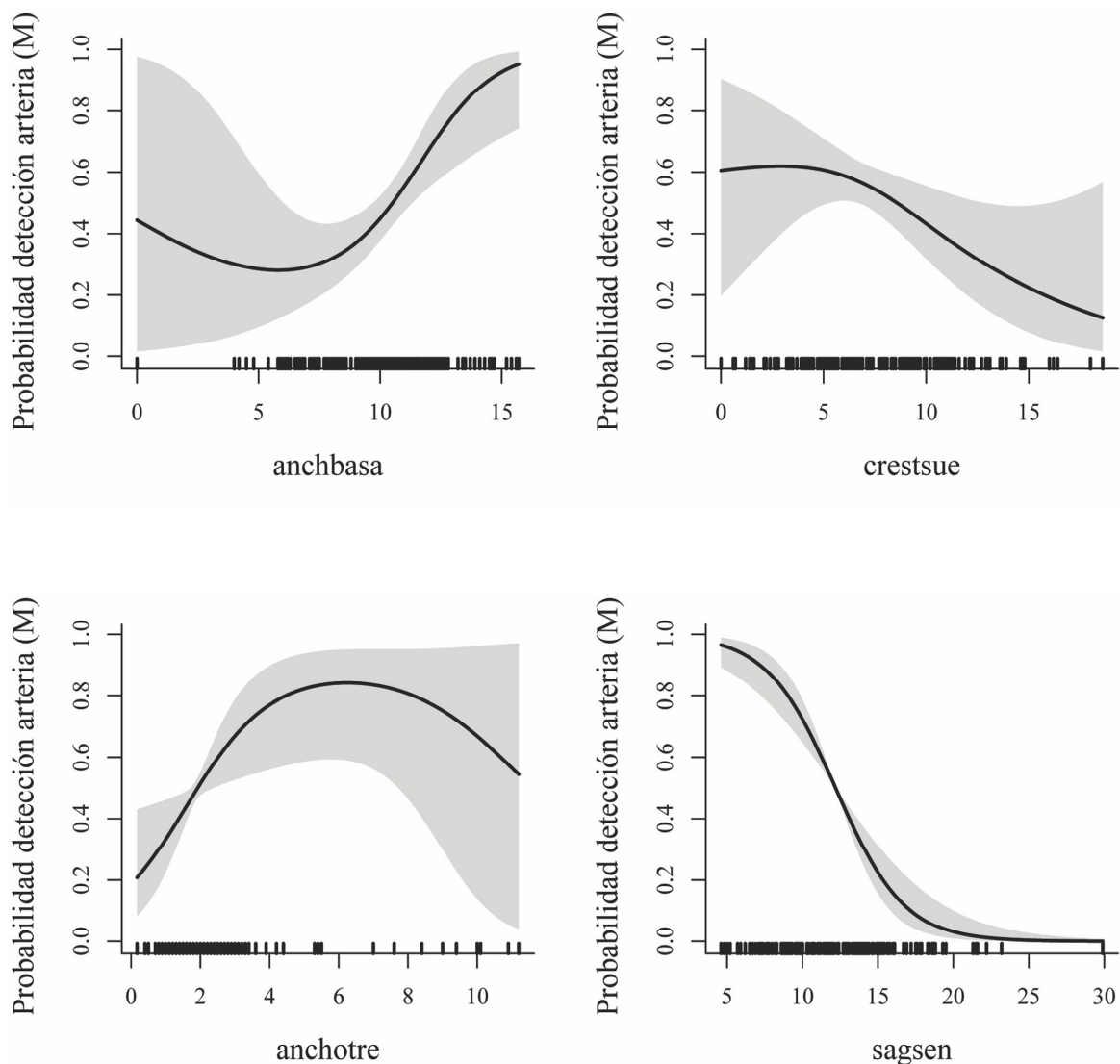
**Tabla 2:** Resultados parte paramétrica modelo univariante (mujeres)

		Estimado	Error estimado	Valor z	Valor p
	Intercept	-0,6992	0,7726	-0,905	0,3654
Tipo de dentición	Parcial vs brecha unitaria	0,8884	0,4751	1,8698	0,0615
	Desdent vs brecha unitaria	1,165	0,8511	1,3687	0,1711
	Parcial vs desdentado	-0,2766	0,7498	-0,3689	0,7122
	Filo vs deprimida	0,195	0,8599	0,2268	0,8206
	Plano vs deprimida	0,4338	0,7187	0,6036	0,5461
	Post-exodoncia vs deprimida	-0,0599	1,0717	-0,0559	0,9554
Tipo de cresta	Redondeada vs deprimida	1,5703	0,7875	1,9941	0,0461
	Plano vs filo de cuchillo	0,2388	0,6983	0,342	0,7323
	Post-exodoncia vs filo de cuchillo	-0,2549	0,9901	-0,2575	0,7968
	Redondeada vs filo de cuchillo	1,3753	0,7028	1,9569	0,0504
	Post-exodoncia vs aplanada	-0,4937	0,8747	-0,5644	0,5725
	Redondeada vs aplanada	1,1365	0,5061	2,2455	0,0247
	Redondeada vs post-exodoncia	1,6302	0,8295	1,9652	0,0494

**Tabla 2** (continuación) parte flexible:

	Edf	Ref. df	Chi. Sq	p-value
s(anchura de la cresta basal)	1,769	1,945	11,160	0,00981 **
s(distancia cresta suelo sinusal)	1,808	2,275	5,326	0,11838
s(ancho pared lateral seno)	1,760	1,941	7,019	0,03246 *
s(anchura sinusal)	1,000	1,000	30,437	3,39e-08 ***

En las mujeres no existen diferencias significativas en la probabilidad de detectar la arteria en función del tipo de dentición. En relación al tipo de cresta, las diferencias se encuentran en las crestas redondeadas, que se asocian con una probabilidad significativamente mayor de detección de la arteria que los otros cuatro tipos de cresta. Además, la anchura basal de la cresta ósea residual se asocia significativamente con la probabilidad de detección de la arteria, aumentando dicha probabilidad para valores de anchura por encima de los 5mm. Lo mismo sucede para la anchura de la pared lateral del seno: la probabilidad aumenta al aumentar la anchura, hasta valores en torno a 4 mm, donde parece mostrar una cierta tendencia al descenso, si bien el intervalo de confianza en esta región es demasiado amplio para que el efecto sea significativo. El efecto más claro se observa en la anchura sagital: la probabilidad de detectar la arteria disminuye de forma pronunciada al aumentar la anchura sagital del seno, siendo prácticamente nula para anchuras por encima de 20 mm (Figura 3).

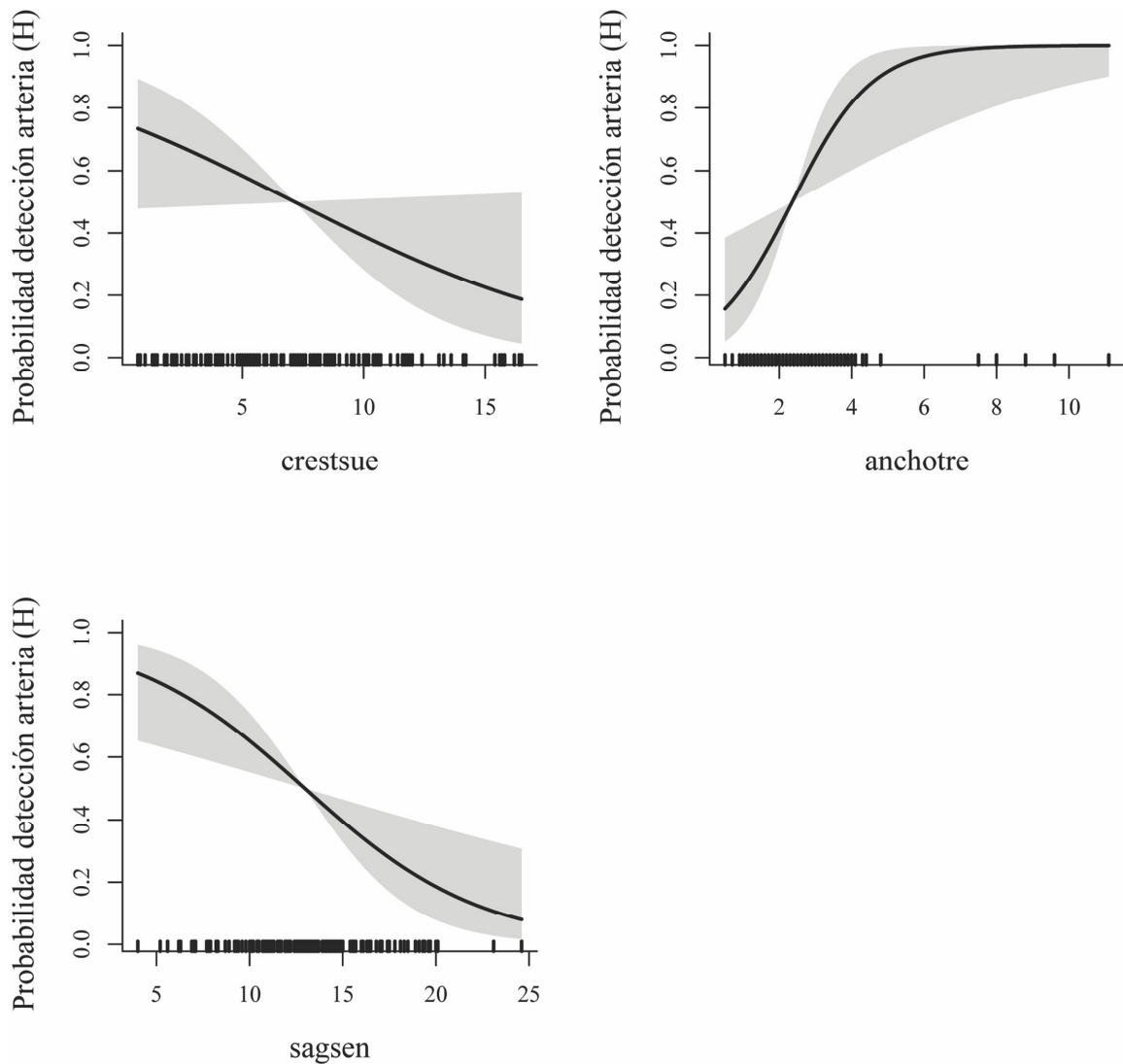


**Figura 3.** Gráficos que representan la probabilidad de detección de la arteria en relación a las co-variables del modelo multivariante para mujeres.

**- Modelo multivariante para hombres**

En los hombres existen diferencias significativas en la probabilidad de detectar la arteria en función del patrón de ausencia de piezas, siendo mayor en los pacientes desdentados que en los que presentan pequeñas brechas edéntulas. Dicha probabilidad también es significativamente superior en crestas post-extracción que en crestas deprimidas o aplanadas.

Al igual que sucedía con las mujeres, la probabilidad de detección aumenta con la achura de la pared lateral del seno hasta valores de aproximadamente 4mm. La anchura sagital del seno muestra una relación inversa con la probabilidad de detección de la arteria, si bien el descenso no es tan intenso como en las mujeres (en éstas, la pendiente es más abrupta) (Figura 4).



**Figura 4.** Gráficos que representan la probabilidad de detección de la arteria en relación a las co-variables del modelo multivariante para hombres.

### **Capacidad de discriminación de los modelos multivariantes**

La capacidad de los modelos obtenidos para discriminar entre la capacidad de detección de la arteria vs. no detección se ha evaluado mediante el valor del área bajo la curva (AUC), obtenido a partir de curvas ROC. El modelo multivariante que incluyen a todos los pacientes tiene una AUC de 0,79, siendo de 0,85 para mujeres, y de 0,79 para hombres. La mayor capacidad de discriminación se obtiene para las mujeres.

### **4.3. Calibre de la arteria alveolar antral y riesgo quirúrgico**

Este apartado tiene como objetivo identificar variables asociadas a pacientes con AAAs de mayor calibre y por tanto de mayor riesgo quirúrgico. Cuando consideramos el calibre arterial como una variable continua, el mejor modelo conteniendo como variable respuesta (Y= calibre de la arteria) es:  $Y = \alpha + \beta_1 \text{ sexo} + \beta_2 \text{ tipo de dentición} + f_1 \text{ (ancho de la pared lateral del seno)} + f_2 \text{ (anchura sinusal)} + f_3 \text{ (área sinusal)} + \text{(distancia cresta-arteria)}$ . El porcentaje de desviación explicada por dicho modelo es del 32 %.

Las mujeres presentan valores significativamente menores que los hombres en el calibre de la arteria. Los pacientes parcialmente desdentados también presentan arterias de menor calibre que los desdentados. Respecto a las variables continuas, las que presentan un mayor efecto son la anchura de la pared lateral del seno y la distancia de la cresta a la arteria. Respecto a la anchura de la pared lateral, al aumentar ésta aumenta significativamente el calibre de la arteria, hasta valores en torno a 4mm. Por encima de este valor, el calibre de la arteria disminuye. En relación a la distancia de la cresta a la arteria, al aumentar ésta, también aumenta significativamente el calibre de la arteria. Además, la anchura sagital del seno solo tiene efecto en un rango concreto de valores (por encima de 7mm y hasta los 15mm), rango en el cual el calibre de la arteria aumenta de manera significativa.

## 5. CONCLUSIONS

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## 5. CONCLUSIONS

1. The prevalence of AAA detection in the sinus lateral bony wall is significantly higher when CBCT explorations are used in comparison with conventional CT radiographic studies. Still, additional comparative studies to control potential confounding factors are required to ascertain the actual diagnostic value of radiographic explorations for assessing the PSAA prior to SLS procedures.
2. The probability of AAA detection by CBCT is influenced by patient's gender (higher in males and for narrow sinuses) and increases with the thickness of the sinus lateral bony wall and the height of the residual alveolar ridge. Particularly in women, the thickness of the ridge at the basal level would seem to improve the explanatory model for AAA detection. With these findings in mind, it is suggested that future studies in this field assess and control for these variables.
3. There is a high proportion of maxillary sinuses where AAA follows a course close to the alveolar crest ( $\leq 15$  mm), which was classically considered a safe distance for SLS. This position is related to the presence of an atrophic crest (depressed ridge form) and wide MS where the distance of the vessel to the floor of the sinus is small. This information may permit better surgical planning for SLS procedures.
4. AAAs which lie away from the bony crest, in subsinusally edentulous male patients whose sinus is about 14mm wide and their lateral wall is 4 mm thick, are likely to be larger and therefore would require careful and detailed surgical planning.



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## 6. REFERENCES

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## 7. PUBLICAITONS FROM PhD DISSERTATION

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UNIVERSIDADE  
DE SANTIAGO  
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## 7. PUBLICAITONS FROM PHD DISSERTATION

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Systematic Review  
 Pre-Implant Surgery

# Detection of the posterior superior alveolar artery in the lateral sinus wall using computed tomography/cone beam computed tomography: a prevalence meta-analysis study and systematic review

**P. Varela-Centelles<sup>1,2</sup>,  
 M. Loira-Gago<sup>1</sup>,  
 J. M. Seoane-Romero<sup>1</sup>,  
 B. Takkouche<sup>3</sup>, L. Monteiro<sup>4</sup>,  
 J. Seoane<sup>1</sup>**

<sup>1</sup>Stomatology Department, School of Medicine and Dentistry, University of Santiago de Compostela, Santiago de Compostela, Spain; <sup>2</sup>EOXI Lugo, Cervo e Monforte de Lemos, Galician Health Service, Lugo, Spain; <sup>3</sup>Department of Preventive Medicine, School of Medicine and Dentistry, University of Santiago de Compostela, Santiago de Compostela, Spain; <sup>4</sup>Medicine and Oral Surgery Department, Dental Sciences Group – Health Sciences Research Centre, Instituto Superior de Ciências da Saúde Norte, CESPU, Paredes, Portugal

*P. Varela-Centelles, M. Loira-Gago, J.M. Seoane-Romero, B. Takkouche, L. Monteiro, J. Seoane: Detection of the posterior superior alveolar artery in the lateral sinus wall using computed tomography/cone beam computed tomography: a prevalence meta-analysis study and systematic review. Int. J. Oral Maxillofac. Surg.* 2015; xxx: xxx–xxx. © 2015 International Association of Oral and Maxillofacial Surgeons. Published by Elsevier Ltd. All rights reserved.

**Abstract.** A systematic search of MEDLINE, Embase, and Proceedings Web of Science was undertaken to assess the prevalence of the posterior superior alveolar artery (PSAA) in the lateral sinus wall in sinus lift patients, as identified using computed tomography (CT)/cone beam computed tomography (CBCT). For inclusion, the article had to report PSAA detection in the bony wall using CT and/or CBCT in patients with subsinus edentulism. Studies on post-mortem findings, mixed samples (living and cadaveric), those presenting pooled results only, or studies performed for a sinus pathology were excluded. Heterogeneity was checked using an adapted version of the DerSimonian and Laird  $Q$  test, and quantified by calculating the proportion of the total variance due to between-study variance ( $R_i$  statistic). Eight hundred and eleven single papers were reviewed and filtered according to the inclusion/exclusion criteria. Ten studies were selected (1647 patients and 2740 maxillary sinuses (study unit)). The pooled prevalence of PSAA was 62.02 (95% confidence interval (CI) 46.33–77.71). CBCT studies detected PSAA more frequently (78.12, 95% CI 61.25–94.98) than CT studies (51.19, 95% CI 42.33–60.05). Conventional CT revealed thicker arteries than CBCT. It is concluded that PSAA detection is more frequent when CBCT explorations are used. Additional comparative studies controlling for potential confounding factors are

needed to ascertain the actual diagnostic value of radiographic explorations for assessing the PSAA prior to sinus floor elevation procedures.

Key words: maxillary sinus; artery; posterior superior alveolar artery; sinus floor elevation; meta-analysis.

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Perforation of the sinus membrane is the most frequently reported intraoperative complication of sinus floor elevation (SFE) procedures, arising in up to 19.5% (range 0–58.3%) of cases.<sup>1</sup> The second most common undesired event is severe bleeding, occurring mostly when performing the antrostomy using rotary instruments.<sup>2</sup> As accidental blood vessel damage may cause massive bleeding,<sup>3</sup> careful surgical planning is paramount,<sup>3,4</sup> particularly because the intraosseous anastomosis between the posterior superior alveolar artery (PSAA) and the infraorbital artery (IOA) has been linked to potential haemorrhagic complications.<sup>5,6</sup> The intraosseous branch of the PSAA within the lateral sinus wall usually describes a straight or U-shaped course,<sup>7</sup> forming a concave arch whose closest point to the osseous crest is located near to the first molar.<sup>8,9</sup> This anastomosis supplies the Schneiderian membrane, periosteum, and the anterolateral sinus wall,<sup>6–10</sup> while contributing to graft integration and healing of the surgical wound.<sup>11</sup>

Accidental damage to these vessels is reported to account for up to 20% of major bleeding events,<sup>4,5</sup> although some case series have described lower incidences.<sup>12</sup> Experimental SFE studies in edentulous cadaveric material have reported that intraosseous arteries are involved in up to 83% of cases when the antrostomy is performed at the level of the first and second molars.<sup>13</sup> As severe postoperative haemorrhages have also been described after transcrestal SFE procedures,<sup>14</sup> the accurate identification of vascular structures before surgery is essential to avoid undesired complications.<sup>12</sup>

Anatomical studies have consistently detected the intraosseous PSAA anastomosis in every maxillary sinus,<sup>5,7,11</sup> but computed tomography (CT) scans have failed to identify these structures in many patients,<sup>5</sup> and their use for this purpose has been discouraged.<sup>15</sup> Nevertheless, multiple imaging studies have been developed since this evidence-based review article was published,<sup>15</sup> showing an increased capability of CT and cone beam computed tomography (CBCT) for detecting the PSAA within the sinus wall.<sup>10</sup> These circumstances appear to justify the need for a

systematic review and meta-analysis aimed at assessing the prevalence of the PSAA in the lateral sinus wall of SFE patients using CT/CBCT.

### Materials and methods

The methods of analysis and the inclusion criteria were detailed in the study protocol to ensure homogeneous criteria amongst all researchers during the study. The aforementioned protocol was initially conceived for radiological identification of the PSAA within the bony sinus wall.

A systematic search was undertaken in July 2014 of MEDLINE, Embase, and Proceedings Web of Science (Conference Proceedings Citation Index-Science; CPCI-S), using the following strategy: ((“blood supply” OR “maxillary artery” OR “arterial supply” OR “vascular”) AND (“maxillary sinus” OR “sinus floor elevation” OR “sinus lift” OR “sinus augmentation”)), with both medical subject headings (MeSH) and free text words. This search strategy was reviewed independently, discussed by all authors, and supplemented with an additional hand-search<sup>16</sup> performed using the library catalogue of the study institution, considering both books and relevant journals (Fig. 1).

Studies were considered if they fulfilled the following eligibility criteria: (1) provided data on the detection of the PSAA anastomosis within the sinus lateral bony wall using CT and/or CBCT; (2) reported on samples of patients with subsinus edentulism. No language restrictions were applied. Studies were excluded if they reported post-mortem findings, used mixed samples (living and cadaveric specimens), presented pooled results only, or were radiographic studies performed for a suspected sinus pathology.

Data were retrieved by two investigators (MLG and JS) in a standardized manner using a custom-made extraction sheet. Disagreements were resolved by consensus.

### Quality assessment

Quality was evaluated by means of a five-item binary scale (yes/no) designed specifically for this study and based upon the

STROBE guidelines for reporting observational studies<sup>17,18</sup>: (1) Does the report give details about study participants? One point if the study detailed adequate demographic information about the sample. (2) Have the aim and the outcome of the study been clearly defined? One point when the aim of the study was clearly stated and the number of outcome events was detailed. (3) Was the sampling frame a true or close representation of the target population? One point if the radiographic examinations were undertaken for SFE purposes. (4) Was the measuring instrument adequately described? One point if the equipment, software, and measuring instruments were clearly stated. (5) Does the report give a cautious overall interpretation of the results? One point when both surgical implications and existing evidence were discussed.

When information on a specific item was not provided by the authors, the item was graded as ‘no’. The quality score was graded independently by two investigators (JS and BT).

### Data analysis

The prevalence of the PSAA in the lateral wall of the maxillary sinus for each study was computed by dividing the number of sinuses in which the artery was detected by the total number of sinuses examined. To determine the 95% confidence intervals (95% CI), the exact method proposed by Newcombe and Altman was used.<sup>19</sup> The study-specific prevalence estimates were then weighted by the inverse of their variance to compute a pooled prevalence and its 95% CI. Both fixed-effects and random-effects pooled estimates were calculated. When heterogeneity is detected, the random-effects model gives more reliable results than the fixed-effects model, including a more conservative (wider) CI. To check for heterogeneity, a version of the DerSimonian and Laird *Q* test, adapted to small samples, was used. To quantify this heterogeneity, the proportion of the total variance due to between-study variance (*Ri* statistic) was calculated.<sup>20</sup> In the meta-analysis, due to the presence of a considerable amount of heterogeneity between studies, the fixed-effects pooled

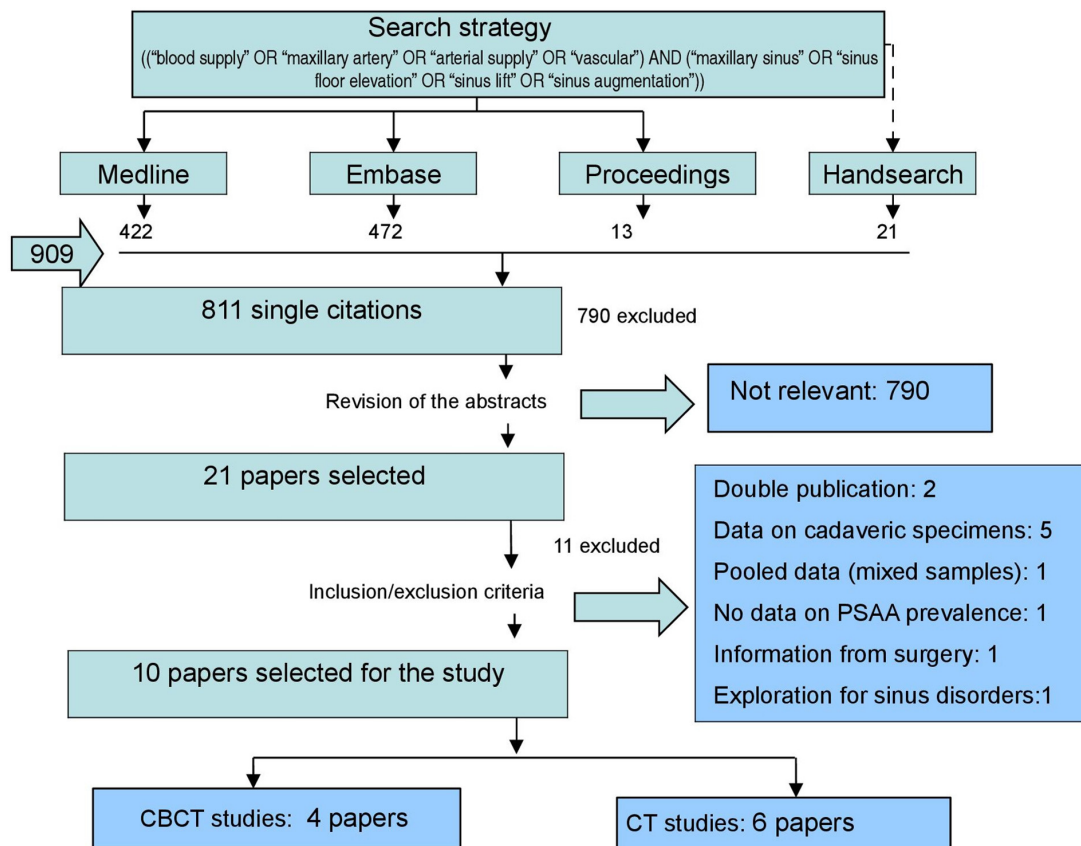


Fig. 1. The search strategy and identification of articles for the meta-analysis.

prevalence figures were considerably overestimated and their 95% CI artificially narrow. Although for the sake of exhaustivity both types of estimate are presented, the random-effects estimates were used as the most appropriate figures. All analyses were performed with the software HEPiMA version 2.1.3.<sup>21</sup>

## Results

The search strategy identified 811 single papers. The abstracts of these papers were reviewed for relevance of the content to the topic of this meta-analysis; 790 were

consequently discarded. Finally, 21 papers were filtered for further analysis according to the eligibility criteria set for the study (Fig. 1).

Eleven reports did not meet the inclusion criterion of considering samples made up of patients with subsinus edentulism; one paper provided pooled data from patients and cadaveric material.<sup>22</sup> Four papers presented data obtained from the same series of cadaveric material: Solar et al.<sup>11</sup> and Traxler et al.<sup>23</sup>; and Yoshida et al.<sup>24</sup> and Sato.<sup>25</sup> Another study, aiming to identify the branches of the maxillary artery, did not provide

information on the prevalence within the sinus lateral bony wall.<sup>26</sup> One more report was discarded because it reported surgical information from a series of cadaveric material,<sup>13</sup> and five articles describing a prevalence of 100% of PSAA within the sinus wall, based on anatomical dissections, were also excluded from this meta-analysis.<sup>6,7,11,25,27</sup> (Table 1). Finally, another paper was discarded because CT scans were performed to investigate sinus disorders.<sup>28</sup>

Ten cross-sectional studies (five Asian,<sup>2,8,9,29,30</sup> three European,<sup>31–33</sup> and two American<sup>5,10</sup>) published during

Table 1. Prevalence of the PSAA in the lateral sinus bony wall, as identified by dissection of cadaveric material.

Author, year	Country	Number (M/F)	Age, years, mean ± SD (min–max)	Maxillary sinus (n)	Prevalence (%)	PSAA diameter, mm, mean ± SD	Distance PSSA to alveolar crest, mean ± SD	Subsinus dental pattern
Solar et al. <sup>11</sup>	Austria	18 (10/8)	67 (55–75)	18	100	1.6 ± 0.2	19.5 ± 3.6	Edentulous
Hur et al. <sup>7</sup>	Korea	42 (18/24)	70 (47–94)	42	100	0.8 ± 0.3	NA	Dentate
Rosano <sup>6</sup>	France	15 (–)	76 (59–90)	30	100	NA	NA	NA
Sato <sup>25</sup>	Japan	19 (–)	77.7 ± 9.8 (59–94)	34	100	NA	NA	Dentate
Kqjiku et al. <sup>27</sup>	Croatia	10 (5/5)	73 ± 13.6 (46–94)	20	100	NA	14.5	Dentate

PSAA, posterior superior alveolar artery; M, male; F, female; SD, standard deviation; NA, not available.

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Table 2. Characterization of patients and studies considered in the meta-analysis.

Author, year	Country	Number (M/F)	Age, years, mean ± SD (min–max)	Maxillary sinus (n)	Type of exploration	Prevalence (95% CI)	PSAA diameter, mm, mean ± SD	Distance PSSA to alveolar crest <sup>a</sup> , mean ± SD	QS
Elian et al. <sup>5</sup>	USA	50 (–)	(–)	100	CT	52.9 (43.12–62.68)	–	16.4 ± 3.5	4
Mardinger et al. <sup>8</sup>	Israel	104 (35/69)	52.9 (24–76)	208	CT	55 (48.24–61.76)	–	16.9 ± 4.4	4
Rosano et al. <sup>33</sup>	Italy	100 (–)	53.5 (29–78)	200	CT	47 (40.08–53.92)	–	11.2 ± 2.9	4
Kim et al. <sup>29</sup>	Korea	200 (–)	57.7 (45–65)	400	CT	52 (47.10–56.90)	1.5 ± 0.4	15.4 ± 4.0	3
Güncü et al. <sup>31</sup>	Turkey	121 (49/72)	48.7 ± 11.8	242	CT	64.5 (58.47–70.53)	1.3 ± 0.5	18.0 ± 4.9	5
Jung et al. <sup>9</sup>	Korea	250 (159/91)	57.1 (33–83)	250	CBCT	52.8 (46.61–58.99)	–	14.7 ± 4.0	4
Anamali et al. <sup>10</sup>	USA	254 (120/134)	57.6 (20–87)	254	CBCT	94.4 (91.57–97.23)	–	–	4
Ilgüy et al. <sup>32</sup>	Turkey	135 (55/80)	43.1 ± 17.5	116	CBCT	75.9 (68.12–83.68)	0.9 ± 0.2	16.8 ± 3.4	4
Kang et al. <sup>2</sup>	Korea	150 (90/60)	49.35 (23–86)	150	CBCT	90 (85.20–94.80)	1.18 ± 0.4	17.03 ± 3.5	4
Yang and Kye <sup>30</sup>	Korea	283 (186/97)	57.1 (18–84)	566	CT	36.5 (32.51–40.62) <sup>a</sup>	–	18.3 ± 0.5 <sup>a</sup>	4

M, male; F, female; SD, standard deviation; CI, confidence interval; PSAA, posterior superior alveolar artery; QS, quality score; CT, computed tomography; CBCT, cone beam computed tomography.

<sup>a</sup>Data obtained from the authors.

the last decade met the eligibility criteria. These reports included a total of 1647 patients and 2740 maxillary sinuses (study unit). Three of these papers obtained their images from SFE preoperative studies,<sup>5,31,33</sup> five reports included CT/CBCT explorations done before implant insertion in the posterior maxilla,<sup>2,8,9,29,30</sup> and the remaining two articles used images of patients with subsinus edentulism retrieved from the files of maxillofacial radiology units<sup>10,32</sup> (Table 2).

The radiographic studies included in this meta-analysis showed a pooled prevalence of PSAA in the lateral wall of the maxillary sinus of 62.02 (95% CI 46.33–77.71) (Table 3). Six of these studies had used CT to identify the intraosseous anastomosis,<sup>5,8,29–31,33</sup> whereas the other four had employed CBCT technology.<sup>2,9,10,32</sup> These latter studies reported higher frequencies of PSAA detection (pooled prevalence of 78.12, 95% CI 61.25–94.98, ranging from 52.8% to 94.4%)<sup>9,10</sup> when compared to CT studies (pooled prevalence 51.19, 95% CI 42.33–60.05).

Radiographic studies using conventional CT revealed an average gauge of the artery higher than reported when CBCT was used. Also, more than 60% of the

sinuses studied with CBCT showed a PSAA <1 mm in diameter,<sup>2,30</sup> with this proportion being lower for sinuses studied by CT.<sup>8,29,31,33</sup>

A wide range of average distances from the artery to the osseous crest was reported (11.2–18.3 mm).<sup>30,33</sup> Except for the three studies with distances lower than 16 mm,<sup>9,29,33</sup> heterogeneity between studies was large. As explained before, the random-effects estimates were the only ones considered acceptable.

Only four studies reported on the mediolateral position of the PSAA in the sinus wall: three of them described a fully intraosseous path for the artery,<sup>2,31,32</sup> while the other frequently identified the vessel in an intra-sinus position between the Schneiderian membrane and the sinus bony wall.<sup>9</sup> In all the series considered, the superficial position of the artery (on the outer cortex of the lateral sinus wall) was the least frequently reported location, with percentages ranging from 5.2% to 7.7% of the sinuses studied.<sup>9,32</sup>

**Discussion**

These results demonstrate that preoperative assessment with CBCT allows a more

frequent and more effective detection of the PSAA than conventional CT. As no clinical trials are available, the data considered in this meta-analysis were obtained from large case-series with an unlikely selection bias. Nevertheless, some of these studies have limitations related to the lack of control for confounding factors, such as age,<sup>5</sup> gender,<sup>5,29,33</sup> and ethnicity, which may compromise their internal validity. Also, the intra-sinus location of the artery may hinder radiological detection and act as an additional confounding factor.<sup>33</sup>

The lower radiological detection of PSAAs (present in 100% of specimens) may be related to their small diameter.<sup>6,8</sup> The average gauge of the arteries detected by CT was found to be markedly higher than that reported from CBCT studies, which may mean that only larger arteries are detected with this approach.<sup>29,31</sup> CBCT has shown better sensitivity and cost-effectiveness for the detection of the PSAA and is recommended as a dose-sparing alternative to conventional CT for maxillofacial imaging.<sup>32</sup>

The need for a preoperative PSAA assessment aside, the relevance of vascular damage during antrostomy is

Table 3. Posterior superior alveolar artery in the lateral wall of the maxillary sinus: pooled prevalence (PP) and 95% confidence intervals (CI).

	Number of studies	PP (95% CI), fixed-effects	PP (95% CI), random-effects	Ri <sup>a</sup>	Q test P-value
All studies	10	73.10 (71.65–74.55)	62.02 (46.33–77.71)	0.99	0.00001
<16 mm	3	51.06 (47.70–54.42)	51.06 (47.70–54.42)	0.00	0.41
≥16 mm	6	60.69 (58.33–63.06)	62.48 (43.62–81.34)	0.98	0.00001
CT	6	48.70 (46.35–51.05)	51.19 (42.33–60.05)	0.93	0.00001
CBCT	4	88.11 (86.26–89.95)	78.12 (61.25–94.98)	0.99	0.00001

CT, computed tomography; CBCT, cone beam computed tomography.

<sup>a</sup>Proportion of total variance due to between-study variance.

size-dependent: section of a small vessel (<1 mm) has a negligible surgical impact,<sup>8</sup> while section of those with larger diameters may hamper visualization and compromise the procedure<sup>12</sup>; thus vessels >3 mm in diameter may be ligated to prevent severe iatrogenesis.<sup>33,34</sup> In this respect, the studies considered in this meta-analysis reported average artery sizes ranging from 0.9 to 1.5 mm,<sup>29,32</sup> with larger diameters linked to male gender<sup>2</sup> and thicker bony walls,<sup>2</sup> and a controversial age influence.<sup>2,8,34</sup>

These circumstances highlight the importance of the distance between the PSAA and the bony crest when designing the anastomosis,<sup>11</sup> since average reported values (although grouped)<sup>2,5,8,9,29,32</sup> are scattered within a wide range of distances (2.8–31.7 mm), probably due to anatomical variations and different vertical ridge dimensions.<sup>2,31</sup> The position of the PSAA should also be taken into account, particularly those with a partial intraosseous location on the inner side of the lateral bony wall, in order to avoid vascular injuries during membrane detachment.<sup>3</sup> This situation was reported to occur in about 13–63.8% of the sinuses analysed.<sup>9,32</sup>

Although there are no significant differences between piezoelectric surgery and conventional rotary instruments in terms of visibility, surgical time, membrane perforation, and patient expectations,<sup>35,36</sup> the use of piezoelectric surgery may be particularly recommended for sinuses with a higher gauge PSAA anastomosis.

Within the inherent limitations and the potential biases of the studies considered in this meta-analysis, it is concluded that the prevalence of PSAA detection in the sinus lateral bony wall is higher when CBCT explorations are used, compared with scores for conventional CT radiographic studies. Additional comparative studies that control for potential confounding factors are needed to ascertain the actual diagnostic value of radiographic explorations for assessing the PSAA prior to SFE procedures.

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#### Patient consent

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Address:  
Juan Seoane  
Cantón Grande 5  
Apt 1º E  
15003 A Coruña  
Spain  
Tel: +34 981 223 033  
E-mail: [juanmanuel.seoane@usc.es](mailto:juanmanuel.seoane@usc.es)



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## Distance of the alveolar antral artery from the alveolar crest. Related factors and surgical considerations in sinus floor elevation

Pablo Varela-Centelles <sup>1,2</sup>, María Loira-Gago <sup>2</sup>, Antonio Gonzalez-Mosquera <sup>2</sup>, Juan M. Seoane-Romero <sup>2</sup>, José M. Garcia-Martin <sup>3</sup>, Juan Seoane <sup>2</sup>

<sup>1</sup> C.S. Praza do Ferrol. EOXI Lugo, Cervo e Monforte de Lemos. Galician Health Service. Pza. Ferrol 11. 27001 Lugo. Spain

<sup>2</sup> Stomatology Department. School of Medicine and Dentistry. University of Santiago de Compostela. Entrerriros s/n. 15782. Santiago de Compostela. A Coruña. Spain

<sup>3</sup> Department of Medicine and Medical-Surgical Specialities. School of Medicine and Health Sciences. University of Oviedo. C/ Julián Clavería s/n. 33006. Oviedo. Spain

Correspondence:  
 Cantón Grande 5, Apt. 1ºE  
 15003 A Coruña  
 Spain  
[juanmanuel.seoane@usc.es](mailto:juanmanuel.seoane@usc.es)

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### Abstract

**Background:** In a variable proportion of maxillary sinuses alveolar antral artery is located close to the residual ridge, increasing the chances for haemorrhagic complications during sinus floor elevation procedures.

**Material and Methods:** Retrospective observational study of CBCT explorations performed for implant-treatment planning. The upper first molar area was selected for this study. The relative uncertainty (standard deviation of the measurement divided by its mean and expressed as a percentage from 0% to 100%) was chosen for determining the observational errors. For modeling the chances of AAA detection, the generalized additive models (GAM) approach was chosen.

**Results:** A total of 240 maxillary sinuses were studied (46.25% males) whose median median age was 58 years old (IQR: 52-66). Univariate models showed that the chances for an AAA-alvelar crest distance  $\leq 15$ mm increase in wider sinuses with lower, subsinusally edentulous crests. When distance is considered as a continuous variable, the best multivariate model showed an explained deviance of 67% and included AAA diameter, distance AAA-sinus floor, sinus width, and shape, height and width of the residual ridge. Thinner AAAs are found closer to the crest (within the  $\leq 15$ mm safe distance).

**Conclusions:** Bearing in mind the inclusion criteria and the limitations of this investigation, it is concluded that there is a high proportion of maxillary sinuses where AAA describes a course close to the alveolar crest ( $\leq 15$ mm), which was classically considered a safe distance for SFE. This position is related to the presence of atrophic crests (depressed ridge form) and wide maxillary sinuses where the distance of the vessel to the floor of the sinus is small. This information may permit a better surgical planning of SFE procedures.

**Key words:** Cone-beam computed tomography, blood vessels, sinus floor augmentation, intraoperative complications.

## Introduction

Although maxillary sinus floor elevation (SFE) by lateral approach is a safe and predictable surgical technique for gaining bony tissue for implant placement, it is not free from intra- and post-operative complications (1,2). The second most frequent of these complications (right after sinus membrane perforation) is bleeding secondary to surgical damage to the alveolar antral artery (AAA) during antrostomy (2).

AAA is an anastomosis of the posterior superior alveolar artery (PSAA) and the infraorbital artery (IOA) located at the anterolateral wall of the sinus with a variable course, which supplies the Schneiderian membrane, the sinus wall, and the periosteum (3). It also contributes to graft integration and to the healing of the surgical wound (2).

A careful surgical planning using cone beam computed tomography (CBCT) has been advocated in an attempt to minimise bleeding complications during SFE. Yet, AAA detection rate by CBCT is 78.1% (95%CI=61.2-94.9) (3), and it has proved unable to disclose small arteries (<0.5mm) and those with an intrasinus or fully extraosseous course (2,3).

In any case, the vascularity of the lateral sinus wall varies widely among individuals (2), being the risk for intrasurgical bleeding higher for larger vessels (>2mm) (2), in severely atrophic ridges, and at the area of the first upper molar where the distance between AAA and the alveolar crest is shorter (4,5).

The upper limit of the antrostomy is directly related to the length of the implant to insert (6,7), and 15mm from the bony crest is considered a safe distance to prevent vascular damage (4,8,9). However, in a variable proportion of maxillary sinuses AAA is located closer to the ridge (9) increasing this way the chances for haemorrhagic complications, particularly for patients whose AAA diameter ranges from 1 to 2 mm where the risk for bleeding could reach 57% (10). Despite this fact, there are no studies focused on identifying factors explaining AAA course variations at the anterolateral sinus wall invading the aforementioned safe-distance. Thus, the aim of this investigation was to identify and model the variables related to patients at risk of iatrogenic bleeding during SFE whose AAAs are located within 15mm of the bony crest.

## Material and Methods

In order to attain the aims of this investigation, a retrospective observational study was designed that met the requirements of the university's Ethics Committee. After obtaining informed consent, the study was carried out from March to November 2015 at the Radiology Unit of the School of Medicine and Dentistry of the University of Santiago de Compostela (Spain).

CBCT explorations were identified using the unit's da-

tabase, and retrieved if fulfilled the inclusion criteria, namely explorations performed for implant-treatment planning in maxillary edentulous or subsinusally edentulous patients, or subjects with (an) upper first molar(s) missing. Exclusion criteria were: poor image quality, sinus disorders or previous history of sinus surgery or grafting. As a result, 240 maxillary sinuses with clearly defined AAA were selected out of 466 sinuses that met the inclusion criteria.

All patients were explored by means of a cone beam CT (I-CAT, 17-19. Imaging Sciences International, 1910 North Penn Toad, Hatfield, USA) with its I-CAT software (Imaging Sciences International) set at a resolution of 0.3 voxels with 8.9 seconds of capture time. According to previous findings (4,5), the course of AAA lies closer to the bony crest at the upper first molar level, so this location was selected for performing the coronal sections used in this study.

Two researchers (ML & AG) used the resources provided by the proprietary software (I-CATvision) to undertake linear measurements in CBCT explorations.

The relative uncertainty (standard deviation of the measurement divided by its mean and expressed as a percentage from 0% to 100%) was chosen for determining the observational errors. The variables considered (with its relative uncertainty) included: distance from AAA to sinus floor (0%), and distance from AAA to alveolar crest (0%).

The outcome variable was "distance of AAA from the bony crest", considered both as continuous and dichotomous (coded as "1" for distances  $\leq 15$ mm -risk for iatrogenic damage- and "0" for higher values). Additional potentially-related co-variables, such as gender, pattern of edentulism (maxillary edentulous, subsinusally edentulous, or upper first molar missing), and course of the artery (fully intraosseous; intrasinus -between the Schneiderian membrane and the sinus bony wall-; or superficial -on the outer cortex of the lateral sinus wall) were also studied. The residual ridge was categorised according to Cawood and Howell (11) as class II: immediately post extraction; class III: well-rounded ridge; class IV: knife-edge ridge; class V: flat ridge; and class VI: depressed ridge form. Other variables considered in this investigation were: thickness of the lateral sinus wall, height of the residual bony crest, width of the residual alveolar ridge (at the basal and crestal levels) and width of the maxillary sinus.

### - Statistical analysis

The study unit for this research was not the patient, but the maxillary sinus. Descriptive statistics are summarised using frequencies for categorical variables and the median and mean (central trend statistics), together with the inter-quartile range (IQR) as spread indicant for the quantitative ones.

For modeling the chances of AAA detection, the gener-

alized additive models (GAM) approach was chosen, as it permits modeling the effect of co-variables in a flexible manner. The best multivariate model is automatically selected.

All analyses were undertaken using the R software (R Core Team, 2015) with the mgv package for GAM modeling.

## Results

A total of 240 maxillary sinuses were studied (111 males, 46.25%, and 129 females, 53.75%). The median age of the participants was 58 years old (IQR: 52-66). The median width of the sinus lateral bony wall was 11.5 mm (IQR: 9.5-4.1), and AAA mostly described a fully intraosseous course within it (n=117; 48.7%) with diameters >1mm in most cases (80.5%).

The main subsinusal bone resorption patterns were the “well-rounded”(class III: 106; 44.17%) and “flat ridge” (class V: 52; 21.63%) types, with less frequent presentations of class II: 21 (8.75%); class IV: 30 (12.5%); and class VI: 31 (12.9%). The median ridge height was 7.40 mm (IQR: 5.27-9.85) (Table 1).

Univariate models have shown a relationship between the AAA-alveolar crest distance and the pattern of edentulousness, bone resorption, height of the residual ridge, distance of AAA to the sinus floor, the sinus area under the artery, and the width of the maxillary sinus. The chances for an AAA-alveolar crest distance  $\leq 15$ mm increase in wider sinuses with lower, subsinusally edentulous crests (Table 2). Yet, when distance is considered as a continuous variable, the best multivariate model showed an explained deviance of 67% and included AAA diameter, distance AAA-sinus floor, sinus width, and shape, height and width of the residual ridge. ( $Y = \alpha + \beta_1$  ridge shape +  $f_1$  (distance from AAA to sinus floor) +  $f_2$  (diameter of AAA) +  $f_3$  (width of the residual alveolar ridge –basal level-) +  $f_4$  (width of the residual alveolar ridge –cresta level-) +  $f_5$  (maxillary sinus width), where  $f_1$  to  $f_5$  represent smooth functions of covariates (Table 3).

The diameter of AAA is significant in the multivariate model, as larger AAAs are found further from the crest whereas thinner AAAs are closer to the crest (within the

**Table 1.** Main features of the sample studied (n=240).

Variables	n	(%)
<b>Gender</b>		
Male	111	46.25
Female	129	53.75
<b>AAA position</b>		
Fully intraosseous	117	48.75
Superficial	8	3.33
Intrasinusal	115	47.91
<b>AAA diameter</b>		
$\leq 1$ mm	47	19.58
$>1 \leq 2$ mm	162	67.50
$>2$ mm	31	12.91
<b>Pattern of edentulousness</b>		
Fully edentulous maxilla	32	13.34
Subsinusal edentulousness	173	72.08
Upper first molar missing	35	14.58
	<b>Mean</b>	<b>Median (IQR)</b>
<b>Age (years)</b>	58.39	58 (52-66)
<b>Diameter of AAA</b>	1.35	1.30 (1.00-1.60)
<b>Distance from AAA to sinus floor (mm)</b>	7.66	7.10 (5.20-9.70)
<b>Distance from AAA to alveolar crest (mm)</b>	15.26	14.90 (12.20-17.50)
<b>Maxillary sinus width (mm)</b>	11.7	11.5 (9.50-14.10)
<b>Thickness of the lateral sinus wall (mm)</b>	2.53	2.0 (1.50-2.70)
<b>Height of the residual alveolar ridge (mm)</b>	7.76	7.40 (5.27-9.85)
<b>Width of the residual alveolar ridge (basal level) (mm)</b>	10.18	10.15 (8.30-12.12)
<b>Width of the residual alveolar ridge (crestal level) (mm)</b>	6.68	6.30 (4.60-8.65)

≤15mm safe distance). AAA are also closer to the ridge when the distance AAA-floor of the sinus is short and the sinus is wide. Contrarily, ridges with less resorption and thus wider at the basal and crestal levels, are significantly linked to a higher course of the vessel (Fig. 1-3).

### Discussion

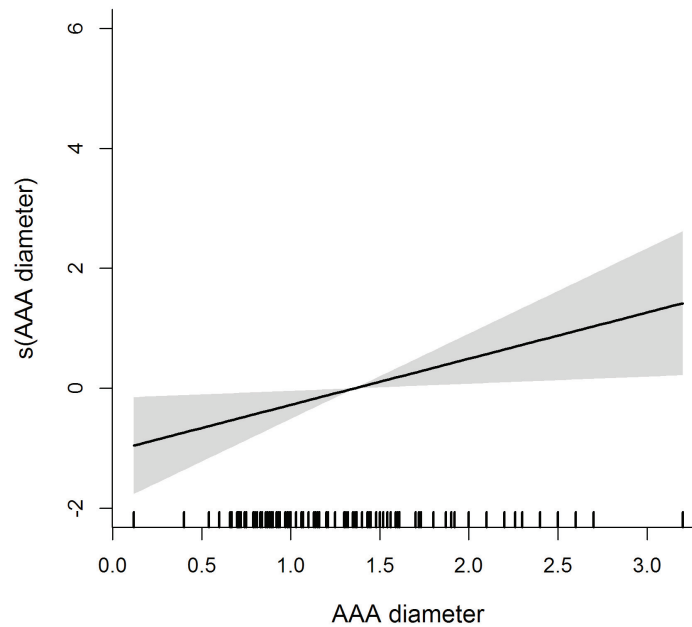
Massive bleeding may occur due to accidental vascular damage during SFE by lateral (12,13) or even transcres-tal approaches (14). Bleeding then results in longer operative times and favour additional complications such

**Table 2.** Univariate GAM logistic models for AAA distance to the bony crest (≤ 15mm vs >15 mm).

Univariate GAM logistic models	Estimate (β )	Standard Error	Z value	p-value	Degrees of freedom (df)	Model's Chi Square	Model's p-value
<b>Gender</b>					1	0.52	0.46
Intercept	0.23	0.19	1.23	0.21			
Female	-0.18	0.25	-0.76	0.46			
<b>Position of AAA</b>					2	3.93	0.14
intercept	-1.94	1.06	-1.82	0.06			
Fully intraosseous	2.13	1.08	1.96	0.04 *			
Intrasinusal	2.13	1.08	1.96	0.04 *			
<b>AAA diameter</b>					2	0.56	0.75
Intercept	0.04	0.29	0.14	0.88			
Diameter (1-2mm)	0.15	0.33	0.46	0.63			
Diameter (> 2 mm)	-0.10	0.46	-0.23	0.81			
<b>Pattern of edentulousness</b> (reference: upper first molar missing)					2	8.01	0.01*
Intercept	1.06	0.38	2.74	0.00			
Fully edentulous maxilla	-1.44	0.52	-2.72	0.00 *			
Subsinusal edentulousness	-1.00	0.41	-2.41	0.01 *			
<b>Classification of posterior maxilla</b> (Reference: depressed ridge form)					4	26.48	2.53e-0.5*
Intercept	1.05	0.41	2.57	0.01			
Class IV (Knife-edge ridge)	-0.78	0.55	-1.42	0.15			
Class V ( Flat ridge)	0.04	0.52	0.08	0.93			
Class II (Post-extraction)	-2.21	0.65	-3.38	0.000 *			
Class III (Well-rounded ridge)	-1.39	0.45	-3.07	0.002 *			
<b>Univariate GAM logistic models</b>				<b>Explained deviance (%)</b>	<b>Effective degrees of freedom (edf)</b>	<b>Model's Chi square</b>	<b>Model's p-value</b>
<b>Age (years)</b>					2.23	6.30	0.09
<b>Thickness of the lateral sinus wall (mm)</b>					1.64	1.84	0.39
<b>Height of the residual alveolar ridge (mm)</b>				20.3	2.10	40.37	1.20e-08 *
<b>Distance from AAA to sinus floor</b>				19.6	2.28	35.83	6.58e-08 *
<b>Width of the residual alveolar ridge (basal level) (mm)</b>					2.84	8.00	0.09
<b>Width of the residual alveolar ridge (crestal level) (mm)</b>					1.00	2.01	0.15
<b>Maxillary sinus width (mm)</b>				2	1.00	6.02	0.01 *
<b>AAA diameter</b>					1.00	1.32	0.24
<b>Sinus area under the artery</b>				7	2.19	12.62	0.004 *

**Table 3.** Multivariate model.

Multivariate	Percentage of deviance explained by the model = 67%							
	Estimate (β)	Standard Error	Z value	p-value	Effective degrees of freedom (edf)	Degrees of freedom (df)	F (Chi square)	Model's p-value
<b>Classification of posterior maxilla</b> (Reference: depressed ridge form)								
Intercept	12.43	0.53	23.14	<2e-16 *		4	19.8	5.3e-16 *
Class IV (Knife-edge ridge)	2.57	0.76	3.36	0.000 *				
Class V ( Flat ridge)	1.24	0.66	1.88	0.06				
Class II (Post-extraction)	3.07	0.84	3.64	0.000*				
Class III (Well-rounded ridge)	4.44	0.61	7.2	8.4e-12 *				
<b>Flexible part of the model (smooth terms)</b>								
AAA diameter					1.00		4.03	0.04 *
Distance from AAA to sinus floor					1.00		299.66	<2e-16 *
Maxillary sinus width					1.72		18.08	2.65e-08 *
Width of the residual alveolar ridge (basal level)					1.54		7.73	0.000 *

**Fig. 1.** Flexible effect of AAA diameter on the distance of the artery to the alveolar crest.

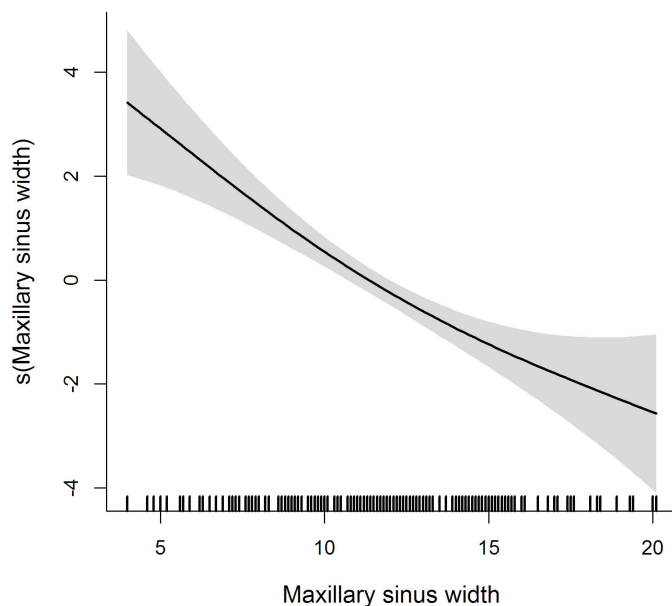


Fig. 2. Flexible effect of maxillary sinus width on AAA distance to the alveolar crest.

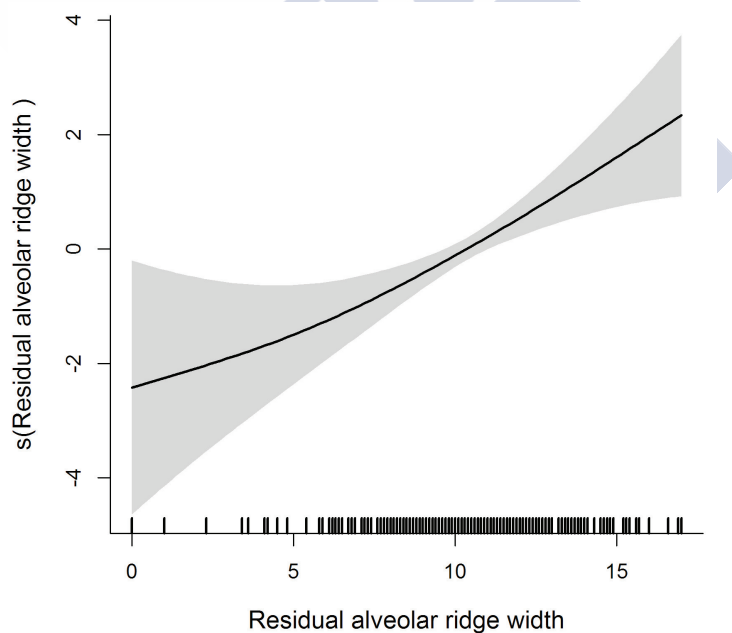


Fig. 3. Flexible effect of width of the residual alveolar ridge on AAA distance to the alveolar crest.

as perforation of the sinus membrane, or reduction of blood supply and displacement of the graft (2). Certain anatomic circumstances, like the diameter and position of the AAA together with the proximity to the alveolar crest may condition the appearance of this kind of com-

plications (3,5). Arteries whose diameter is below 1mm are not a problem (15), but those larger than 2mm may represent a risk for bleeding (2). In this sense, AAA is reported to present an average diameter ranging from 0.9 mm to 15 mm (16). Our findings are consistent with

previous reports, with values about 1.3 mm that resulted to be >1 mm in 80% of the sinuses.

The position of the vessel regarding the lateral wall of the sinus also seems to influence the surgical moment with higher risk for haemorrhage. Thus, intrasinus AAAs located between the sinus membrane and the bony wall makes critical the process of membrane detachment (9). This situation has been reported as the second most common (3,5) and accounts for 47.9% in our series. When the vessel follows a superficial course, external to the lateral wall of the sinus, the risk for haemorrhage would be higher when making the incisions, but not only during antrostomy (4). This location does not reach 8% in any case series (9,16-18). Previous reports acknowledge AAA mostly describes a fully intraosseous course in the sinus lateral bony wall (9,16,17), which occurred in 48.7% of the sinuses in our study.

The location of AAA in relation to the alveolar ridge also influences osteotomy, with reported average distances from 11.2 mm (19) to 18.3 mm (20). The variations in extreme values are wider -2.8 mm to 31.7 mm- (9,17), probably due to variations in the height of the residual ridge and in the distance AAA-floor of the maxillary sinus. Our results show a mean value of 15.2 mm for an average AAA-sinus floor distance of 7.6 mm. Besides, and despite a moderate (20-31%) proportion of cases where AAA invades the safe distance of  $\leq 15$ mm (9,21), our data revealed this phenomenon occurs in up to 48.6% of cases. Thus, this variable should always be taken into account when undertaking SFE procedures.

This investigation has permitted the identification of risk profiles where patients with depressed ridges and sagittally wider sinuses have higher chances for a course of AAA invading the safety distance reported in the literature. On the other hand, patients with rounded and wide alveolar crests whose AAA are identified at more than 6 mm from the sinus floor would be at lower risk for bleeding complications. Moreover, larger arteries tend to locate farther from the bony crest with less probability for iatrogenic damage.

#### - Surgical recommendations

Surgical planning based upon clinical records and CBCT explorations, and the use of piezoelectric devices for osteotomy permits a reduction of the surgical risk (5). Some authors have suggested ligating arteries >3 mm to prevent severe iatrogenesis (18,20,21). Alternative specific techniques (double window) may also be used to avoid AAA during antrostomy and reducing the risk for bleeding (3,5). In those situations where AAA describes a mainly intrasinus course, the process of detachment and elevation of the Schneiderian membrane should be particularly careful. When the course of the vessel is fully extraosseous, the risk for bleeding accidents is related to the incision and flap design.

#### Conclusions

Bearing in mind the inclusion criteria and the limitations of this investigation, it is concluded that there is a high proportion of maxillary sinuses where AAA describes a course close to the alveolar crest ( $\leq 15$ mm), which was classically considered a safe distance for SFE. This position is related to the presence of atrophic crests (depressed ridge form) and wide maxillary sinuses where the distance of the vessel to the floor of the sinus is small. This information may permit a better surgical planning of SFE procedures.

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**Conflict of Interest**

The authors have declared that no conflict of interest exist.





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## Short communication

## Diameter of alveolar antral artery in the lateral sinus wall: study of related factors

P. Varela-Centelles<sup>a,b</sup>, J. Seoane<sup>b,\*</sup>, M. Loira-Gago<sup>b</sup>, A. González-Mosquera<sup>b</sup>,  
J.M. Seoane-Romero<sup>b</sup>

<sup>a</sup> C.S. Praza do Ferrol, EOXI Lugo, Cervo, e Monforte de Lemos, Galician Health Service, Pza Ferrol 11, 27001 Lugo, Spain

<sup>b</sup> Stomatology Department, School of Medicine and Dentistry, University of Santiago de Compostela, C/Entrerriós s/n, 15782 Santiago de Compostela, A Coruña, Spain

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### Abstract

To identify the variables that influence the diameter of the artery in the lateral sinus wall, we studied 240 sinuses, focusing on sex, pattern of tooth loss, type of residual crest, thickness of the lateral wall, height and width of the ridge, and width of the sinus.

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*Keywords:* cone-beam computed tomography; blood vessels; sinus floor augmentation; intraoperative complications

### Introduction

The alveolar antral artery, which is an anastomosis of the posterior superior alveolar and infraorbital arteries, runs through the anterolateral wall of the maxillary sinus to ensure blood supply to the wall itself, the periosteum, and the sinus membrane.<sup>1,2</sup> Operations such as the Le Fort I osteotomy, or the Caldwell-Luc anastomosis, and maxillary fractures may affect it.<sup>3</sup> When the sinus floor is raised, bleeding may displace the graft and compromise its integration.<sup>4</sup>

To the best of our knowledge, there are no publications on this topic, even though the identification of patients at risk of bleeding (in the larger alveolar antral artery) would be useful. The aim of our study was to identify variables related to the diameter of the alveolar antral artery in the lateral sinus wall.

### Material and methods

This study is a secondary analysis of a subsample of 240 maxillary sinuses selected from 466 that had been investigated for implant-supported prostheses within a retrospective observational study. We obtained approval from the university Ethics Committee.

Patients were examined using cone-beam computed tomography (CT) (I-CAT, 17-19. Imaging Sciences International, Hatfield PA, USA). The coronal sections were obtained at the first upper molar area (given the vicinity of the artery to the alveolar ridge).<sup>1</sup> We examined the diameter of the vessel and the covariates were sex, pattern of tooth loss, type of residual crest,<sup>5</sup> thickness of the lateral sinus wall, height of the residual ridge, and width of the ridge and the sinus.

\* Correspondence to: Cantón Grande 5, Apt 1ºE, 15003 A Coruña, Spain, Tel.: +34 981 223 033.

E-mail address: [juanmanuel.seoane@usc.es](mailto:juanmanuel.seoane@usc.es) (J. Seoane).

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Table 1  
Multivariate model. Factors related to the diameter of the alveolar antral artery. Percentage of deviance explained by the model = 32%.

Parametric part of the model	Estimate (β)	Standard error	Z value	Effective degrees of freedom	Degrees of freedom	F (chi square)	p value	Model's p value
Intercept	1.53	0.07	19.40		1	14.24	2.10 <sup>-16</sup>	0.000
Sex								
Female	-0.19	0.05	-3.56				0.000	0.03
Pattern of edentulousness					2	3.42	0.45	
Fully edentulous maxilla compared with upper first molar missing	0.07	0.10	0.74					
Subsinusal edentulousness compared with upper first molar missing	-0.11	0.07	-1.51				0.13	
Subsinusal edentulousness compared with fully edentulous maxilla	-0.18	0.07	-2.36				0.01	
Flexible part of the model (smooth terms)								
Thickness of the lateral sinus Wall (mm)				3.16		7.61		1.99.10 <sup>-5</sup>
Distance from the alveolar antral artery to the sinus floor (mm)				1.00		7.41		0.006
Width of the maxillary sinus (mm)				3.84		2.51		0.04
Sinus area under the artery (mm)				3.66		2.79		0.03

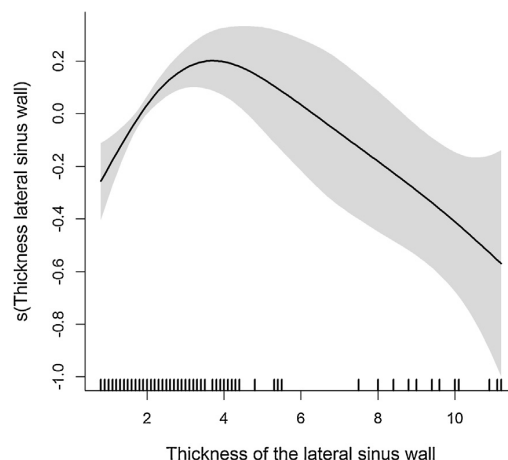


Fig. 1. Flexible effect of the thickness of the wall on the diameter of the alveolar antral artery.

**Statistical analysis**

We modelled the probability for alveolar antral artery diameter using logistic generalised additive models (GAM) with the R software (The R Foundation, Vienna, Austria) and the mixed GAM computation vehicle (mgcv) package for GAM modelling. GAM are extensions of Generalised Linear Models in which the linear functions are replaced by (unknown) flexible functions. The interpretation of GAM is simple since the flexible effect of the covariate directly reflects the association between this covariate and the response.

**Results**

In the sample of 240 maxillary sinuses (n=111 men = 46.25%), median (IQR) age was 58 (52-66) years. The median (IQR) diameter was 1.30 (1.00 - 1.60)mm. The alveolar antral artery mainly followed an intraosseous course (n=117; 48.75%) with gauges ranged from 1 to 2 mm (n = 162; 67.50%).

When Y = diameter of the artery, the best multivariate model was:  $Y = \alpha + \beta_1 \text{ sex} + \beta_2 \text{ (pattern of tooth loss)} + f_1 \text{ (thickness of the lateral wall)} + f_3 \text{ (sinusal area under the artery)} + f_4 \text{ (distance between the alveolar antral artery and the alveolar crest)}$ . This model explains a deviance of 32%. Men had appreciably larger vessels than women.

When considered as continuous variables, both the distance between the alveolar antral artery and the bony crest, and the thickness of the lateral wall, had a crucial effect on the gauge of the artery. This effect for a large vessel increased with the distance from the crest. The same phenomenon occurred with a lateral wall up to 4 mm thick. Beyond this value, the effect decreases (Fig. 1). The wider the maxillary sinus, the more likely it is to find a large alveolar antral artery,

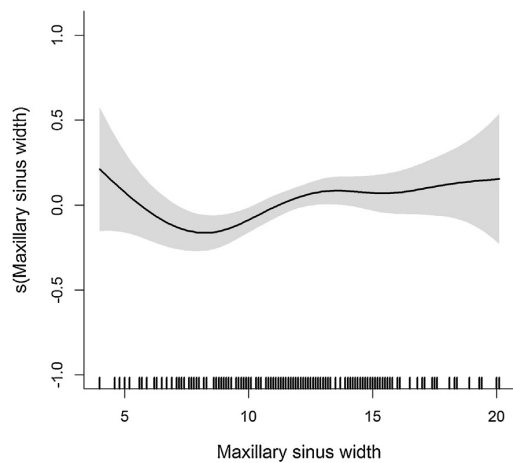


Fig. 2. Flexible effect of the width of the sinus on the diameter of the alveolar antral artery.

although this effect is only true for narrow sinuses (7–14 mm) (Fig. 2, Table 1).

## Discussion

The diameter of the alveolar antral artery shows wide variations.<sup>4,6</sup> The risk for perioperative bleeding for diameters between 1 and 2 mm is about 57% when the sinus floor is being lifted,<sup>5</sup> which increases for diameters of more than 2 mm.<sup>4,7</sup>

The sex of the patient and the thickness of the lateral wall have been independently related to the diameter of the alveolar antral artery.<sup>8,9</sup> Our study with flexible models has shown that the association with the thickness of the sinus wall only occurs for values up to 4 mm, and also that the width of the maxillary sinus is related to the diameter of the alveolar antral artery for values between 7 mm and 14 mm.

We concluded that arteries are likely to be larger in men whose sinuses are about 14 mm wide with lateral walls about 4 mm thick, and their course is likely to be away from the bony crest, so careful surgical planning is required.

## Conflict of interest

We have no conflicts of interest.

## Ethics statement/confirmation of patient's permission

We obtained approval from the university Ethics Committee was obtained and permission from the patient was not applicable.

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