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Review Article

The Importance of Oral Health Providers in the Management and Support of the Head and Neck Cancer Patients

Mayara Santos de Castro² and Marta Miyazawa^{1*}

- ¹Department of Clinic and Surgery, School of Dentistry, Federal University of Alfenas, 700 Gabriel Monteiro da Silva Street, Alfenas, Brazil ²Oncology Resident (Stomatology). A.C. Camargo Cancer Center, 211 Professor Antônio Prudente Street, São Paulo, Brazil
- *Corresponding Author: Marta Miyazawa, Department of Clinic and Surgery, School of Dentistry, Federal University of Alfenas, 700 Gabriel Monteiro da Silva Street, Alfenas, Brazil.

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Abstract

This article aims to present important considerations and recommendations based on reviewed articles retrieved on PubMed database and guidelines for head and neck cancer patients for management and support before, during and after oncologic treatment, in order to maintain oral health, prevent, evaluate and treat side effects, improve quality of life and survival. Therefore, it is evident the vital importance of oral health providers for the oncologic treatment success of head and neck cancer patients.

Keywords: Head and Neck Cancer; Oral Cancer; Oral Health; Oncologic Treatment; Quality of Life

Introduction

The role of oral health providers in the management of head and neck cancer patients covers a wide range of services from diagnosis through survivorship [1]; before, during and after oncologic treatment there is the risk of developing significant side effects that may affect the hard and soft tissue of the oral cavity and impair the quality of life of these patients [2]. To minimize this risk, a careful clinical oral evaluation and a well-integrated management plan within the overall oncologic treatment plan from the initiation of therapy is required [1,2]. Therefore, this article aims to present considerations and recommendations based on available literature for the management and support of the head and neck patients, in order to maintain oral health, prepare for oncologic treatment consequences, improve quality of life and survival.

Material and Methods

An electronic search was conducted from January 1979 to October 2018 using the PubMed/Medline, Science Direct, and Web of Science databases. The keywords selected according to Medical Subject Heading (MeSH) terms were as follows: management AND oral cancer OR head and neck cancer; support AND oral cancer OR head and neck cancer; oral health providers AND oral cancer OR head and neck cancer; and dentistry AND oral cancer OR head and neck cancer. Articles were eligible under the following inclu-

sion criteria: English language; full-text available; population: head and neck cancer patients; intervention: oral health providers in the management and support of the head and neck cancer patients; and study design: review articles, clinical trials, controlled trials, retrospective studies, and case reports. The exclusion criteria adopted were as follows: articles published in any other language than English; and full-text not available. In that way, 39 relevant articles were selected and used in our manuscript.

Early diagnosis

When head and neck cancer is diagnosed early, the patient may have a better subsequent quality of life and higher survival rates; the opposite can be applied to patients with late diagnosis [3]. Therefore, it is of vital importance dentists to be able to effectively identify the first signs and symptoms of this condition [4]. The squamous cell carcinoma (SCC) is the most frequent malignant neoplasm in the head and neck region; it corresponds to more than 90% of oral malignant neoplasms in the oral cavity [5]. The classical clinical presentation of oral SCC is an ulcer, which can be superficial, endophytic (ulcero-infiltrative) or exophytic (ulcero-vegetative); in addition to the ulcerated forms, oral SCC can also appear as a leucoplasic, erythroplasic or erythroleucoplasic plaque; a radiographic radiolucency "in moth eaten appearance" can be observed with irregular and nondefined borders when there is bone involvement [4,6,7].

In that way, observing such clinical features in the patient's oral cavity, the incisional biopsy should be performed and with the histopathological confirmation of malignant neoplasm, the patient should be referred to the head and neck surgeon in order to evaluate the possibility of surgical resection with safety margins and the oncologist will verify the need for adjuvant radiotherapy and/or chemotherapy [4]. These treatment modalities such as surgery, radiotherapy, and chemotherapy, alone or in combination, may result in significant acute and chronic changes of the oral cavity that will require adequate management and support by dentists [1,2].

Oral evaluation pre-radiotherapy and/or chemotherapy

Prior to the initiation of radiotherapy and/or chemotherapy, a careful clinical examination of the patient's oral cavity should be performed, in addition to a radiographic evaluation, in order to oral adequation for oncologic treatment, eliminating foci of infection, performing necessary dental extractions with at least 14 days before the start of radiotherapy to allow healing and prevent osteoradionecrosis, endodontic treatments, removal of dental caries, and accomplishment of satisfactory restorations (glass ionomer can be used, which releases fluoride), periodontal treatment, removal of bone spicules and exostoses susceptible to trauma, treatment of odontogenic cysts and tumors, and adjustments of maladaptive prostheses and/or the confection of new prostheses (also for the prevention of osteorradionecrosis) [8,9].

The patient should also be oriented and clarified about the possible side effects of oncological treatment in the oral cavity, such as oral mucositis (OM), xerostomia, opportunistic infections, trismus, dysphagia, and odynophagia, radiation caries, and mainly about the risk of osteoradionecrosis of the jaws related to dental surgical procedures performed during and/or after radiotherapy [10]. Preventive measures of such side effects should be presented and if possible instituted, improving the quality of life of the patient, allowing the maintenance of adequate oral food intake and giving support for the continuation of the radiotherapy and/or chemotherapy sessions without interruption of the oncologic treatment for the resolution of acute, painful and debilitating problems that can interfere in the final treatment result and patient's survival [1,11,12].

Head and neck patients' follow-up during and after radiotherapy and/or chemotherapy

Prevention and treatment of oral mucositis

OM is a severe complication of highdose radiotherapy and chemotherapy for head and neck cancer [11,12]; it manifests as pain-

ful mucosal erythema with or without ulceration, predominantly affecting non-keratinized oral tissues [2,8]. OM can be classified by the World Health Organization (WHO) mucositis scale according to signs and symptoms on a 0-4 scale: grade 0 - no mucositis symptoms; grade 1 - oral soreness and erythema; grade 2 - oral erythema, ulcers and tolerates solid diet; grade 3 - oral ulcers and tolerates liquid diet; and, grade 4 - impossibility of oral food intake [13,14]. Next we will present important recommendations in the management of OM in head and neck cancer patients.

Good oral hygiene

Pre-existing oral bacterial colonization is associated with OM and increases risk of local and systemic infections; thus, maintenance of good oral hygiene is essential during oncologic treatment [13,15]. Patients should follow an oral care protocol including soft brushing with fluoride toothpaste, maintenance of a soft, non-cariogenic diet, minimize denture use, saline rinse, and avoidance of smoking [8,13,16].

Intraoral stents

Studies have reported that the use of intraoral stents in patients with oral cancer has presented favorable results in preventing unnecessary radiation doses to normal tissues adjacent to cancer and reducing oral complications of oncologic treatment, such as OM [17-19]. These intraoral stents are designed to open the oral cavity and exclude healthy structures from the radiation field; besides, they are able to immobilize the jaw and tongue, effectively recreating the same position during planning and all subsequent treatment sessions of radiotherapy [17-19]. Such devices may be made of acrylic resin after molding the patient's upper and lower arcade and bite registration in order to assemble the models into an articulator [17-19].

Photobiomodulation

The Multinational Association of Supportive Care in Cancer (MASCC) and International Society of Supportive Care in Cancer (ISOO) recommend the photobiomodulation (PBM) as an effective treatment for OM [16]. These groups also recommended that PBM to be used to prevent OM [12,16]. The PBM is effective for accelerating wound repair and tissue regeneration [20]. It has been shown that PBM influences different phases of wound healing: *the inflammatory phase* - immune cells migrate to the site of tissue injury; the *proliferative phase* - stimulation of fibroblasts and macrophages as well as other repair components; and, the *remodeling phase* - collagen deposition and rebuilding of the extracellular matrix at the wound site [20,21].

Based on the literature [12,21] and on our experience, it is proposed the following PBM preventive protocol for OM: start the PBM therapy from the first day of radiotherapy and continue during all days of radiotherapy (no requirement regarding the timing of PBM sessions, before or after radiotherapy sessions) [12]. For chemotherapy with agents that may possibly cause OM [such as 5-fluorouracil (5-FU), EXTREME, and high doses of methotrexate (MTX)], the PBM preventive protocol can also be performed as follows: start the PBM therapy from the first day of chemotherapy and continue during all the course of chemotherapy [12].

The following PBM parameters showed efficacy: wavelength = 660 nm; average power = 40 mW; beam area = 0.04 cm²; irradiance = 1 W/cm²; time per point = 10 s; energy = 0.4 J; and, fluence = 10 J/cm2 [21]. During each intraoral PBM session, the tip of the laser pen should be positioned perpendicular to the predetermined points of different sites of the oral mucosa, being 10 s of irradiation per point. These sites consist of oral commissures (1 point for each commissure), lips mucosae (3 points for each lip), buccal mucosae (3 points for each side), lateral borders of the tongue (3 points for each side), ventral tongue (2 points), anterior floor of the mouth (2 points), and soft palate (2 points) [21]. In case of appearance of OM, the same parameters should be used in points distributed throughout the extension of the lesion [12,21]. PBM therapy was never delivered over a tumor site [21].

Oral mucositis pain control

Topical local anesthetics (such as topical lidocaine and benzocaine lozenges) have been shown to be effective in OM mild pain control [8,22]. The MASCC and ISOO recommend the use of 2% morphine mouthwash in alleviating mucositis-related pain [16,23]. Other commonly used agents are Gelclair, corticosteroid rinses, sucralfate, pentoxyfylline, granulocyte-macrophage-colony-stimulating factor, and anticholinergic agents have limited evidence supporting its use [8,24-26]. Benzydamine hydrochloride has evidence of benefit with radiation dosages < 50 Gy, but there is insufficient and conflicting evidence for its use in patients with > 50 Gy [8,27,28].

Opportunistic infections

Oropharyngeal candidiasis (OPC) is the most common opportunistic infection in head and neck cancer patients [2]. OPC is associated with burning sensation and pain in the oral mucosae, taste change and can extend to the esophagus, resulting in dysphagia and odynophagia; systemic dissemination may occur in immunocompromised patients [2]. Clinical oral presentation includes pseudomembranous candidiasis (thrush) with removable

white plaques, erythematous candidiasis, and angular cheilitis [2]. Topical oral treatments are recommended as first-line therapy in milder forms of candidiasis [2,29]. Instructions include making mouthwash with nystatin four to six times daily, maintaining contact time on the mucosa as long as possible, and then swallowing if the patient is not diabetic. Topical miconazole is available in cream form, and in a muco-adhesive tablet that has a broad spectrum of activity against Candida species, being interesting its use in cases of angular cheilitis [2,29].

Systemic treatments should be used in case of failure of topical treatment or immediately with severe OPC in high risk (immunocompromised) patients [2,30]. The Infectious Diseases Society of America recommends 200 mg on day one (loading dose) followed by 100 mg/day for OPC [30]. Fluconazole can be used for prophylaxis in cases with frequent recurrences using 50-200 mg/day or 100-400 mg/week [30,31]. However, the widespread use of fluconazole has been associated with the emergence of fluconazole resistant fungae [31]. Voriconazole and posaconazole have demonstrated efficacy in esophageal candidiasis in immunocompromised patients [2].

Xerostomia

"Dry mouth" is the most common complaint of patients who have received radiotherapy in head and neck region; due to radiation-induced damage to salivary glands, more than 90% of the patient's present xerostomia [32]. Modern radiotherapy techniques, such as intensity-modulated radiotherpy (IMRT), are able to spare a large volume of the salivary glands, have been developed, however does not yet cover the entire population [33]. The attempt to restore patients' salivary flow may be made with various pharmacotherapies, such as muscarinic-cholinergic agonists that stimulate salivary flow and alleviate symptoms without significant side effects [8,34]. If salivary gland stimulation fails with medication, therapy with the use of artificial saliva can be started to provide greater patient comfort; salivary replacement rinses, Oral Balance gel and Biotene toothpaste, carboxymethylcellulose, carmellose and mucin sprays, polyacrylic acid, and sugarless gum improve symptoms [8,35].

Radiation caries

Head and neck cancer patients present an increased risk of dental caries following radiotherapy primarily due to hyposalivation [2]. Saliva has essential functions in maintaining tooth structure due to control of pH, remineralization and antimicrobial and tooth cleansing effects [36]. Radiation caries develop more rapidly and are more likely to include nonclassical surfaces of teeth (gum line

cavities and cusp tips) when compared to classical caries; untreated radiation caries can progress rapidly and cause pain, infection of the jaw bone, and potential need for tooth extraction, resulting in risk of osteoradionecrosis [2].

All patients who have received radiotherapy in head and neck region should be placed on a strict, high-fluoride regimen to help prevention of dental demineralization [8,37]. In case of permanent hyposalivation, fluoride therapy must be continued indefinitely [8]. The recommendations reported in the literature include: daily 2.2% or 3% NaF rinse, application of 1% NaF gel every second day via custom trays, daily 0.4% stannous fluoride application, and twice daily 1.1% NaF toothpaste. All these methods are effective, however, the fluoride gel with custom trays have shown to be the most reliable in its ability to prevent post-radiation dental caries [37]. Early detection of caries through dental follow-up visits every 6 months are recommended to preserve oral health [2,8]. More frequent follow-ups may be necessary depending on persistence of hyposalivation and the presence/progression of dental demineralization, caries, and periodontal status [2,8].

Oral rehabilitation of the patient

The surgical resection of the oral cancer can result in considerable mutilation of patient; therefore, dentists also have an important role in oral rehabilitation and in the significant improvement of the quality of life of these patients [38,39]. Bucomaxillofacial prostheses, such as palatal obturator prostheses, as well as osseointegrated implants, can improve swallowing and chewing of food, phonation and aesthetics [38,39].

Conclusion

Oral health providers have a vital importance in the management and support of the head and neck cancer patients, preventing, assessing, and treating oral complications before, during and after oncologic treatment, which will reflect as better quality of life for the patient and better survival rates.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Bibliography

- Sroussi HY, Jessri M, Epstein J. Oral Assessment and Management of the Head and Neck Cancer Patient. Oral Maxillofac Surg Clin North Am. 2018;S1042-3699.
- Sroussi HY, Epstein JB, Bensadoun RJ, Saunders DP, Lalla RV, Migliorati CA, Heaivilin N, Zumsteg ZS. Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. Cancer Med. 2017;6(12):2918-2931.
- 3. Akbulut N, Oztas B, Kursun S, Evirgen S., et al. Delayed diagnosis of oral squamous cell carcinoma: a case series. J Med Case Rep. 2011;6:291-294.
- de Castro MS, de Carli ML, Pereira AAC, Sperandio FF, Hanemann JAC. Failure to deal with the early signs of oral squamous cell carcinoma leads to its delayed diagnosis: A case series. Open J Clin Med Case Rep. 2017;3:1242-1249.
- American Cancer Society. Cancer Facts and Figures 2016. Atlanta: American Cancer Society. 2016.
- Pires FR, Ramos AB, Oliveira JB, Tavares AS, Luz PS, Santos TC.
 Oral squamous cell carcinoma: clinicopathological features from 346 cases from a single Oral Pathology service during an 8-year period. J Appl Oral Sci. 2013;21(5):460-467.
- Tamgadge S, Tamgadge A, Modak N, Bhalerao S. Primary intraosseous squamous cell carcinoma arising from an odontogenic keratocyst: a case report and literature review. Ecancermedical science. 2013;9:316-324.
- Kufta K, Forman M, Swisher-McClure S, Sollecito TP, Panchal N. Pre-Radiation dental considerations and management for head and neck cancer patients. Oral Oncol. 2018;76:42-51.
- 9. Georgopoulos R, Liu JC. Examination of the patient with head and neck cancer. Surg Oncol Clin N Am. 2015;24(3):409-421.
- 10. Mod D, Mod H, Jha AK. Oral and dental complications of head and neck radiotherapy and their management. J Nepal Health Res Counc. 2013;11(25):300-304.
- 11. Villa A, Sonis ST. Mucositis: pathobiology and management. Curr Opin Oncol. 2015;27(3):159-164.

- 12. Brandão TB, Morais-Faria K, Ribeiro ACP, Rivera C, Salvajoli JV, Lopes MA, Epstein JB, Arany PR, de Castro G Jr, Migliorati CA, Santos-Silva AR. Locally advanced oral squamous cell carcinoma patients treated with photobiomodulation for prevention of oral mucositis: retrospective outcomes and safety analyses. Support Care Cancer. 2018;26(7):2417-2423.
- 13. Maria OM, Eliopoulos N, Muanza T. Radiation-induced oral mucositis. Front Oncol. 2017;7:89.
- 14. World Health Organization, WHO Handbook for Reporting Results of Cancer Treatment, WHO Handbook. 1979;15-22.
- Kostler WJ, Hejna M, Wenzel C, Zielinski CC. Oral mucositis complicating chemotherapy and/or radiotherapy: options for prevention and treatment. CA Cancer J Clin. 2001;51(5):290-315.
- 16. Lalla RV, Bowen J, Barasch A, Elting L, Epstein J, Keefe DM, McGuire DB, Migliorati C, Nicolatou-Galitis O, Peterson DE, Raber-Durlacher JE, Sonis ST, Elad S; Mucositis Guidelines Leadership Group of the Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISOO). MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer. 2014;120(10):1453-1461.
- Rocha BA, Lima LMC, Paranaíba LMR, Martinez ADS, Pires MBO, de Freitas EM, Vilas Boas CV, de Melo Filho MR. Intraoral stents in preventing adverse radiotherapeutic effects in lip cancer patients. Rep Pract Oncol Radiother. 2017;22(6):450-454.
- Verrone JR, Alves FA, Prado JD, Boccaletti KW, Sereno MP, Silva ML, Jaguar GC. Impact of intraoral stent on the side effects of radiotherapy for oral cancer. Head Neck. 2013;35(7):E213-217.
- 19. Verrone JR, Alves FA, Prado JD, Marcicano A, de Assis Pellizzon AC, Damascena AS, Jaguar GC. Benefits of an intraoral stent in decreasing the irradiation dose to oral healthy tissue: dosimetric and clinical features. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;118(5):573-578.
- Avci P, Gupta A, Sadasivam M, Vecchio D, Pam Z, Pam N, Hamblin MR. Low-level laser (light) therapy (LLLT) in skin: stimulating, healing, restoring. Semin Cutan Med Surg. 2013;32(1):41-52.
- Bensadoun RJ. Photobiomodulation or low-level laser therapy in the management of cancer therapy-induced mucositis, dermatitis and lymphedema. Curr Opin Oncol. 2018;30(4):226-232.

- 22. Su YX, Benedek GA, Sieg P, Liao GQ, Dendorfer A, Meller B, Rades D, Klinger M, Hakim SG. Radioprotective effect of lidocaine on neurotransmitter agonist-induced secretion in irradiated salivary glands. PLoS ONE. 2013;8(3):e60256.
- 23. Sarvizadeh M, Hemati S, Meidani M, Ashouri M, Roayaei M, Shahsanai A. Morphine mouthwash for the management of oral mucositis in patients with head and neck cancer. Adv Biomed Res. 2015;4:44.
- 24. Barber C, Powell R, Ellis A, Hewett J. Comparing pain control and ability to eat and drink with standard therapy vs Gelclair: a preliminary, double centre, randomised controlled trial on patients with radiotherapy-induced oral mucositis. Support Care Cancer. 2007;15(4):427-440.
- 25. Nicolatou-Galitis O, Sarri T, Bowen J, Di Palma M, Kouloulias VE, Niscola P, Riesenbeck D, Stokman M, Tissing W, Yeoh E, Elad S, Lalla RV. Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). Systematic review of anti-inflammatory agents for the management of oral mucositis in cancer patients. Support Care Cancer. 2013;21(11):3179-3189.
- 26. Saunders DP, Epstein JB, Elad S, Allemano J, Bossi P, van de Wetering MD, Rao NG, Potting C, Cheng KK, Freidank A, Brennan MT, Bowen J, Dennis K, Lalla RV. Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO). Systematic review of antimicrobials, mucosal coating agents, anesthetics, and analgesics for the management of oral mucositis in cancer patients. Support Care Cancer. 2013;21(11):3191-3207.
- 27. Roopashri G, Jayanthi K, Guruprasad R. Efficacy of benzydamine hydrochloride, chlorhexidine, and povidone iodine in the treatment of oral mucositis among patients undergoing radiotherapy in head and neck malignancies: a drug trail. Contemp Clin Dent. 2011;2(1):8-12.
- 28. Epstein JB, Silverman Jr. S, Paggiarino DA, Crockett S, Schubert MM, Senzer NN, Lockhart PB, Gallagher MJ, Peterson DE, Leveque FG. Benzydamine HCl for prophylaxis of radiation-induced oral mucositis: results from a multicenter, randomized, double-blind, placebo-controlled clinical trial. Cancer. 2001;92.4:875-885.

- 29. Bensadoun RJ, Daoud J, El Gueddari B, Bastit L, Gourmet R, Rosikon A, Allavena C, Céruse P, Calais G, Attali P. Comparison of the efficacy and safety of miconazole Lauriad® tablets to those of miconazole gel in the treatment of oropharyngeal candidiasis: a controlled multicenter, randomised, phase III trial in patients treated with radiotherapy for head and neck cancer. Cancer. 2008;112(1):204-211.
- 30. Pappas, PG, Kauffman CA, Andes D, Benjamin DK Jr, Calandra TF, Edwards JE Jr, Filler SG, Fisher JF, Kullberg BJ, Ostrosky-Zeichner L, Reboli AC, Rex JH, Walsh TJ, Sobel JD. Infectious Diseases Society of America. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;48(5):503-535.
- Mann PA, McNicholas PM, Chau AS, Patel R, Mendrick C, Ullmann AJ, Cornely OA, Patino H, Black TA. Impact of antifungal prophylaxis on colonization and azole susceptibility of Candida species. Antimicrob Agents Chemother. 2009;53(12):5026-5034.
- 32. Beech N, Robinson S, Porceddu S, Batstone M. Dental management of patients irradiated for head and neck cancer. Aust Dent J. 2014;59(1):20-28.
- 33. Pow EH, Kwong DL, McMillan AS, Wong MC, Sham JS, Leung LH, Leung WK. Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: Initial report on a randomized controlled clinical trial. Int J Radiat Oncol Biol Phys. 2006;66(4):981-991.
- 34. Gorsky M, Epstein JB, Parry J, Epstein MS, Le ND, Silverman Jr. S. The efficacy of pilocarpine and bethanechol upon saliva production in cancer patients with hyposalivation following radiation therapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004;97(2):190-195.
- 35. Epstein JB, Emerton S, Le ND, Stevenson-Moore P. A double-blind crossover trial of Oral Balance gel and Biotene tooth-paste versus placebo in patients with xerostomia following radiation therapy. Oral Oncol. 1999;35(2):132-137.
- 36. Dowd, F. J. Saliva and dental caries. Dent Clin North Am. 1999;43(4):579-597.

- 37. Horiot JC, Schraub S, Bone MC, Bain Y, Ramadier J, Chaplain G, et al. Dental preservation in patients irradiated for head and neck tumours: a 10-year experience with topical fluoride and a randomized trial between two fluoridation methods. Radiother Oncol. 1983;1(1):77-82.
- 38. Rocío Barrios, Manuel Bravo, Jose Antonio Gil-Montoya, Ildefonso Martínez-Lara, Blas García-Medina, Georgios Tsakos. Oral and general health-related quality of life in patients treated for oral cancer compared to control group. Health Qual Life Outcomes. 2015;13:9.
- 39. Rocío Barrios, Javier Montero, Miguel A. González-Moles, Pilar Baca, Manuel Bravo. Levels of scientific evidence of the quality of life in patients treated for oral cancer. Med Oral Patol Oral Cir Bucal. 2013;18(4):e578–e584.

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