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### **Radiation-Induced Xerostomia**

# Xérostomie post-radique : évaluation de l'acupuncture

*Articles connexes*: - évaluation dans la xérostomie en général - évaluation de la pharmacopée chinoise -

### **1. Systematic Reviews and Meta-Analysis**

### 1.1. Khamdi 2024

Khamdi S, Matangkasombut O, Lam-Ubol A. Non-pharmacologic interventions for management of radiation-induced dry mouth: A systematic review. Oral Dis. 2024 Jul;30(5):2876-2893. https://doi.org/10.1111/odi.14804

Objectives	Radiation-induced dry mouth negatively impacts patients' oral health and quality of life. Currently, evidence-based recommendation for non-pharmacologic interventions is still lacking. This study aimed to systematically review clinical trials evaluating the efficacy of non-pharmacologic interventions in cancer patients with radiation-induced dry mouth.
Methods	Randomized controlled trials from 2000 were searched from 4 databases, including MEDLINE, Cochrane, Embase via OVID, and SCOPUS, up to December 16th, 2022 (PROSPERO registration CRD42022378405). The risk of bias was assessed using the revised Cochrane risk of bias assessment tool.
Results	Twenty-one studies were included: 11 on artificial saliva, 4 on electrical nerve stimulation (TENS), <b>2 on acupuncture</b> , and one study each on low-level laser therapy, stem cells, chewing gum, and probiotics. Overall bias was low, medium, and high in 33%, 48%, and 19% of the studies, respectively. Certain artificial saliva products and TENS were shown to improve dry mouth symptoms and salivary flow rate (SFR). One study showed that stem cell transplantation significantly increased SFR.
Conclusion	The evidence suggested that certain artificial saliva products and TENS are promising management. However, the evidence was still limited due to heterogeneity of interventions and outcome measurements. Thus, future studies using standard measurements and long-term follow-up are warranted.

#### 1.2. Bonomo 2022

Bonomo P, Stocchi G, Caini S, Desideri I, Santarlasci V, Becherini C, Limatola V, Locatello LG, Mannelli G, Spinelli G, Guido C, Livi L. Acupuncture for radiation-induced toxicity in head and neck squamous cell carcinoma: a systematic review based on PICO criteria. Eur Arch Otorhinolaryngol. 2022 Apr;279(4):2083-2097. https://doi.org/10.1007/s00405-021-07002-1

Purpose	In head and neck squamous cell carcinoma (HNSCC), the potential mitigating effect of complementary medicine interventions such as acupuncture for radiation-induced toxicity is unknown. This study aimed to assess the impact of acupuncture on the incidence and degree of severity of common radiation-induced side effects.
Methods	In accordance with pre-specified PICO criteria, a systematic review was performed. Two electronic databases (Medline and Embase) were searched over a 10-year time frame (01/01/10 to 30/09/20). Patients undergoing a curatively intended, radiation-based treatment for histologically confirmed squamous cell carcinoma of the nasopharynx, oropharynx, larynx, hypopharynx and oral cavity represented the target population of our study. Accurate information on the acupuncture methodology was reported. All included articles were evaluated to identify any potential source of bias RESULTS: Five papers were included in our qualitative analysis, for a total of 633 subjects. Compliance to per-protocol defined schedule of acupuncture sessions was high, ranging from 82 to 95.9%. Most patients (70.6%) were randomly allocated to receive acupuncture for its potential preventive effect on xerostomia. The large heterogeneity in study settings and clinical outcomes prevented from performing a cumulative quantitative analysis, thus no definitive recommendations can be provided.
Conclusions	Although shown to be feasible and safe, no firm evidence currently supports the use of acupuncture for the routine management of radiation-induced toxicity in HNSCC.

### 1.3. NI 2020 🕸

Ni X, Tian T, Chen D, Liu L, Li X, Li F, Liang F, Zhao L. Acupuncture for Radiation-Induced Xerostomia in Cancer Patients: A Systematic Review and Meta-Analysis. Integr Cancer Ther. 2020 Jan-Dec;19:1534735420980825. doi]

Background	Radiation-induced xerostomia is one of the most common symptoms experienced by cancer patients. The aim of our study is to evaluate the preventive and therapeutic effect of acupuncture for radiation-induced xerostomia in cancer patients.
Methods	Eight databases were searched for all published randomized clinical trials (RCTs) on acupuncture for radiation-induced xerostomia in cancer patients up to December 31, 2019. Manual searching included other conference abstracts and reference lists. Meta- analysis was conducted using Revman V.5.3, and risks of bias for included studies was assessed following the Cochrane Handbook.
Results	Eight clinical trials (725 participants) were analyzed, and 3 were included in a meta- analysis. All included trials had a high risk of bias, such as selection, performance, and detection bias. Analysis indicated favorable effects of acupuncture regarding the improvement of xerostomia symptoms (MD -3.05, P = 0.02, 95% CI -5.58 to -0.52), compared with sham acupuncture. There were no significant differences between real acupuncture and sham acupuncture regarding the stimulated salivary flow rate (MD 0.37, P = 0.08, 95% CI -0.05 to 0.79) and unstimulated salivary flow rate (MD 0.09, P = 0.12, 95% CI -0.02 to 0.21), which were whole salivary flow rate. Compared with no acupuncture (standard oral care, usual care, or no treatment), acupuncture produced a significant improvement in patient-reported xerostomia, without causing serious adverse effects. However, a Grading of Recommended Assessments analysis revealed that the quality of all acupuncture outcome measures was low.
Conclusions	The present meta-analysis and systematic review suggests that <b>acupuncture is</b> <b>effective at improving xerostomia symptoms in cancer patients but not at</b> <b>objective salivary flow measurements</b> . The evidence is still limited due to the low quality of the published studies.

### 1.4. Mercadante 2017 Ø

Mercadante V, Al Hamad A, Lodi G, Porter S, Fedele S. Interventions for the management of radiotherapy-induced xerostomia and hyposalivation: A systematic review and meta-analysis. Oral Oncol. 2017;66:64-74. [10221].

	Salivary gland hypofunction is a common and permanent adverse effect of
Introduction	radiotherapy to the head and neck. Randomised trials of available treatment modalities have produced unclear results and offer little reliable guidance for clinicians to inform evidence-based therapy. We have undertaken this systematic review and meta-analysis to estimate the effectiveness of available interventions for radiotherapy- induced xerostomia and hyposalivation.
Methods	We searched MEDLINE, Cochrane Central, EMBASE, AMED, and CINAHL database through July 2016 for randomised controlled trials comparing any topical or systemic intervention to active and/or non-active controls for the treatment of radiotherapy- induced xerostomia. The results of clinically and statistically homogenous studies were pooled and meta-analyzed.
Results	1732 patients from twenty studies were included in the systematic review. Interventions included systemic or topical pilocarpine, systemic cevimeline, saliva substitutes/mouthcare systems, hyperthermic humidification, <b>acupuncture</b> , <b>acupuncture-like transcutaneous electrical nerve stimulation</b> , low-level laser therapy and herbal medicine. Results from the meta-analysis, which included six studies, suggest that both cevimeline and pilocarpine can reduce xerostomia symptoms and increase salivary flow compared to placebo, although some aspects of the relevant effect size, duration of the benefit, and clinical meaningfulness remain unclear. With regard to interventions not included in the meta-analysis, we found no evidence, or very weak evidence, that they can reduce xerostomia symptoms or increase salivary flow in this population.
Conclusions	Pilocarpine and cevimeline should represent the first line of therapy in head and neck cancer survivors with radiotherapy-induced xerostomia and hyposalivation. The use of other treatment modalities cannot be supported on the basis of current evidence.

#### **1.5. Garcia 2015** ☆

Garcia M , Niemtzow RC, McQuade J, Haddad R, Lee R, Spano M, Cohen L. Acupuncture for xerostomia in patients with cancer: An update. Medical Acupuncture. 2015; 27(3):158-67. [188884]

Background	Xerostomia (dry mouth) is a common side-effect of cancer treatment following radiotherapy, especially in patients with head-and-neck (HN) cancer.
Objective	The purpose of this review was to evaluate evidence related to acupuncture for xerostomia in patients with HN cancer.
Materials and Methods	Embase, Medline, Cochrane (all databases), PubMed, and Scopus were searched from inception through December 2014 for studies published in English that were randomized controlled trials (RCTs) evaluating acupuncture to treat and/or prevent xerostomia in patients with cancer. A usual-care and/or placebo comparison group was required for inclusion. Risk of bias (ROB) was rated as low, high, or unclear according to Cochrane criteria. Outcomes and treatment parameters were summarized.

Results	Of 184 articles identified, 136 duplicates were omitted, leaving 48 publications that were screened. Thirty-nine studies were excluded because they were not prospective RCTs of acupuncture in patients with cancer, and three studies did not involve needle insertion into acupuncture points. <b>Six studies met all inclusion</b> <b>criteria</b> . Four investigated acupuncture to treat xerostomia, and two investigated acupuncture to prevent xerostomia. Of the six included trials, four reported significant between-group differences in favor of real acupuncture, and two reported significant within-group differences only. No studies were rated as low ROB, either because of low statistical power or a lack of blinding.
Conclusion	<ul> <li>Acupuncture may be a helpful adjunct to cancer care for treatment and/or prevention of xerostomia in patients with HN cancer, but studies to date have been limited by small sample size and/or lack of blinding. Large phase III trials are currently underway.</li> </ul>

### 1.6. Lovelace 2014 Ø

Lovelace TL, Fox NF, Sood AJ, Nguyen SA, Day Ta. Management of radiotherapy-induced salivary hypofunction and consequent xerostomia in patients with oral or head and neck cancer: meta-analysis and literature review. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014. 117(5):595-607. [178881].

Objective	To analyze the efficacy of various treatment options for radiation-induced hyposalivation in patients with head and neck cancer.
Methods	Study design: A literature review and meta-analysis was performed on all appropriate literature identified via MEDLINE/PubMed.
Results	Fourteen articles were identified that met inclusion criteria for review, and 8 articles qualified for inclusion in the meta-analysis. The available literature addressed both objective and subjective responses of hyposalivation, xerostomia, or both to cholinergic agonists (such as pilocarpine and cevimeline), salivary substitutes, hyperbaric oxygen, and acupuncture.
Conclusions	This analysis indicated that cholinergic agonists were more effective in treating radiation-induced hyposalivation compared with salivary substitutes, hyperbaric oxygen, and acupuncture. However, other treatment modalities, such as salivary substitutes and hyperbaric oxygen, were also found to subjectively improve patients' perception of xerostomia.

### 1.7. Zhuang 2012 Ø

Zhuang L, Yang Z, Zeng X, Zhua X, Chen Z, Liu L, Meng Z. The preventive and therapeutic effect of acupuncture for radiation-induced xerostomia in patients with head and neck cancer: a systematic review. Integr Cancer Ther. 2012. [159293].

Background	Methods: Some studies suggest that acupuncture may be beneficial.
Objectives	The authors evaluated the preventive and therapeutic effect of acupuncture for radiation-induced xerostomia among patients with head and neck cancer.
Methods	PUBMED, EMBASE, Cochrane Library, CBM, CAJD, Wan Fang database, and VIP Database for Chinese Technical Periodicals were electronically searched, in conjunction with further manual search for relevant articles. Studies that met the inclusion criteria were systematically evaluated.

Results	Three randomized controlled trials (RCTs) investigating the therapeutic effect of acupuncture were included. One RCT on the preventive effect of acupuncture was found. Because of the considerable variation among included studies, meta-analysis was not possible. Two included RCTs used placebo controls, and both observed significant improvement in the salivary flow rates between acupuncture and control groups. However, no significant differences were found. Three included RCTs suggested that acupuncture for radiation-induced xerostomia can improve patients' subjective symptoms. The only study evaluating the preventive effect of acupuncture for radiation-induced and stimulated) and dry mouth -related symptoms. Acupuncture treatment was well tolerated by all patients and no severe adverse effects were seen.
Conclusions	Insufficient evidence is available to judge whether acupuncture is safe and whether it is effective in preventing or treating radiation-induced xerostomia. Significant research remains to be done before acupuncture can be recommended for routine use in radiation-induced xerostomia.

### 1.8. Jensen 2010 🕁

Jensen SB et al. A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: Management strategies and economic impact. Support Care Cancer. 2010; 18(8):1061-79. [155308].155308

Objectifs	This systematic review aimed to assess the literature for management strategies and economic impact of salivary gland hypofunction and xerostomia induced by cancer therapies and to determine the quality of evidence-based management recommendations.
Méthode	The electronic databases of MEDLINE/PubMed and EMBASE were searched for articles published in English since the 1989 NIH Development Consensus Conference on the Oral Complications of Cancer Therapies until 2008 inclusive. For each article, two independent reviewers extracted information regarding study design, study population, interventions, outcome measures, results, and conclusions.
Résultats	Seventy-two interventional studies met the inclusion criteria. In addition, 49 intensity- modulated radiation therapy (IMRT) studies were included as a management strategy aiming for less salivary gland damage. Management guideline recommendations were drawn up for IMRT, amifostine, muscarinic agonist stimulation, oral mucosal lubricants, acupuncture, and submandibular gland transfer.
Conclusions	There is evidence that salivary gland hypofunction and xerostomia induced by cancer therapies can be prevented or symptoms be minimized to some degree, depending on the type of cancer treatment. Management guideline recommendations are provided for IMRT, amifostine, muscarinic agonist stimulation, oral mucosal lubricants, acupuncture, and submandibular gland transfer. Fields of sparse literature identified included effects of gustatory and masticatory stimulation, specific oral mucosal lubricant formulas, submandibular gland transfer, acupuncture, hyperbaric oxygen treatment, management strategies in pediatric cancer populations, and the economic consequences of salivary gland hypofunction and xerostomia.

### 1.9. O'Sullivan 2010 Ø

O'sullivan EM, Higginson IJ. Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review. Acupuncture in Medicine. 2010. 28(4):191-9. [158385].

Background	Irradiation-induced xerostomia seriously reduces quality of life for patients with head and neck cancer (HNC). Anecdotal evidence suggests that acupuncture may be beneficial.
Objective	To systematically review evidence on clinical effectiveness and safety of acupuncture in irradiation-induced xerostomia in patients with HNC.
Methods	A detailed search was performed to identify randomised controlled trials (RCTs) and systematic reviews of RCTs on acupuncture in irradiation-induced xerostomia, using AMED, BNIA, CINAHL, Cochrane, Embase, HPSI, PsycInfo and Medline. Grey literature was explored and 11 journals hand searched. Search terms included: acupuncture, xerostomia, salivary hypofunction, hyposalivation, dry mouth, radiotherapy, irradiation, brachytherapy, external beam. Two authors independently extracted data for analysis using predefined selection criteria and quality indicators.
Results	43 of the 61 articles identified were excluded on title/abstract. 18 articles underwent full-text review; three were deemed eligible for inclusion. Two trials had moderate risk of bias; one had high risk. Two trials compared acupuncture with sham acupuncture; one control arm received 'usual care'. Outcome measurements included salivary flow rates (SFRs) in two trials and subjective questionnaires in three. All three trials reported significant reduction in xerostomia versus baseline SFR (p<0.05); one reported greater effect in the intervention group for stimulated SFR (p<0.01). Subjective assessment reported significant differences between real acupuncture and control in two trials (p<0.02-0.05). Insufficient evidence was presented to undertake risk/benefit assessment.
Conclusions	Limited evidence suggests that acupuncture is beneficial for irradiation-induced xerostomia. Although current evidence is insufficient to recommend this intervention, it is sufficient to justify further studies. Highlighted methodological limitations must be dealt with.

### 2. Overview of systematic reviews

### 2.1. Hubner 2022 Ø

Hubner J, Dorfler J, Freuding M, Zaiser C, Buntzel J, Keinki C, Käsmann L. Methodological Review: Summary of Findings for Acupuncture as Treatment for Cancer Therapy-induced Xerostomia. In Vivo. 2022 Nov-Dec;36(6):2579-2597. https://doi.org/10.21873/invivo.12993

Background/aim	With a rapidly growing number of studies, systematic reviews (SRs) and meta- analyses (MAs) on acupuncture, the level of evidence seems to be high. Yet, traditional Chinese acupuncture is built on concepts which are not in accordance with science-based medicine. Accordingly, our aim was to critically assess the evidence presented in SRs and MAs on xerostomia induced by treatment of head and neck cancer with radiotherapy.
Materials and Methods	In February 2022, a systematic search of five electronic databases (Embase, Cochrane, PsychInfo, CINAHL and Medline) was conducted to find SRs/MAs on acupuncture use against cancer-treatment induced xerostomia. We evaluated all SRs/MAs using the AMSTAR instrument, comparing the assessment of the individual studies included and the conclusions drawn by the authors. In case of heterogeneity between the SRs, we evaluated the controversial items of the assessments directly from the studies.
Results	Finally, <b>eight SRs/Mas</b> were included. Most of them show methodological drawbacks in several domains of the AMSTAR instrument, which influences the credibility of the results.

Conclusion	The evidence on the use of acupuncture as treatment for radiotherapy-induced xerostomia is low. Present SRs/MAs mainly summarize results of a few and
	mostly small studies. Even though the included studies greatly overlap, the guality of the presentation and interpretation of the authors differs greatly
	Therefore, a high quality and conclusive summary of the present evidence on
	the use of acupuncture to treat radiotherapy induced xerostomia is still missing.

### **3. Clinical Practice Guidelines**

 $\oplus$  positive recommendation (regardless of the level of evidence reported)  $\emptyset$  negative recommendation (or lack of evidence)

# **3.1.** Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO) 2024 Ø

Hong C, Jensen SB, Vissink A, Bonomo P, Santos-Silva AR, Gueiros LA, Epstein JB, Elad S. MASCC/ISOO Clinical Practice Statement: Management of salivary gland hypofunction and xerostomia in cancer patients. Support Care Cancer. 2024 Jul 25;32(8):548. https://doi.org/10.1007/s00520-024-08688-9

There are a few randomized controlled trials evaluating the use of **acupuncture**, photobiomodulation, salivary gland ductal irrigation/dilation in alleviating salivary gland hypofunction and/or xerostomia. However, the recommendation for their routine use in the clinical setting is premature mainly because of conflicting evidence and the heterogeneities in treatment protocols.

# 3.2. Association of the Scientific Medical Societies, German Cancer Society, German Cancer Aid, (AWMF, DKG, DK, Germany) 2021 ⊕

S3-Leitlinie Komplementärmedizin in der Behandlung von onkologischen PatientInnen. September 2021. https://www.leitlinienprogramm-onkologie.de/leitlinien/komplementaermedizin/

11.3.1.14. Xerostomia. Acupuncture. Recommendation strength: Can. Patient context: Patients with head and neck tumors. Note: During radio/chemotherapy. **Acupuncture**. Recommendation strength: Can. Patient context: Oncological patients .Note: Xerostomia after adjuvant radiotherapy.

# 3.3. Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) / American Society of Clinical Oncology (ASCO, USA) 2021 ⊕

Mercadante V, Jensen SB, Smith DK, Bohlke K, Bauman J, Brennan MT, Coppes RP, Jessen N, Malhotra NK, Murphy B, Rosenthal DI, Vissink A, Wu J, Saunders DP, Peterson DE. Salivary Gland Hypofunction and/or Xerostomia Induced by Nonsurgical Cancer Therapies: ISOO/MASCC/ASCO Guideline. J Clin Oncol. 2021:JCO2101208. [219405].doi

Recommendation 1.3. Acupuncture may be offered during radiation therapy for head and neck cancer to reduce the risk of developing xerostomia (type: evidence-based; evidence quality: intermediate; strength of recommendation: moderate). Recommendation 2.4. Acupuncture may be offered after radiation therapy in patients with head and neck cancer for improvement of xerostomia (type: evidence-based; evidence quality: low; strength of recommendation: weak). Recommendation 2.5. Transcutaneous electrostimulation or acupuncture-like transcutaneous electrostimulation of the salivary glands may be offered after radiation therapy in patients with head and neck cancer for improvement of salivary gland hypofunction and xerostomia (type: evidence-based; evidence quality: low; strength of recommendation: weak).

# 3.4. Association of the Scientific Medical Societies, German Cancer Society, German Cancer Aid, (AWMF, DKG, DK, Germany) 2020 ⊕

Supportive Therapie bei onkologischen PatientInnen. Leitlinienprogramm Onkologie. Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF. 2020. [219443].

https://www.leitlinienprogramm-onkologie.de/fileadmin/user\_upload/Downloads/Leitlinien/Supportivth erapie/LL\_Supportiv\_Langversion\_1.3.pdf

*Xerostomia*. The prophylactic use of classical **acupuncture** therapy improves subjective and objective parameters of radiogenic xerostomia. It can be used. **Acupuncture** can improve the subjective parameters of xerostomia and can be used.

## 3.5. Association Francophone des Soins Oncologiques de Support (AFSOS, France) 2014 $\ensuremath{\oplus}$

Association Francophone des Soins Oncologiques de Support (AFSOS). Fiches Réferentiels : L'acupuncture en onco-hématologie MAJ 2014 (online)

*Xérostomie post-radique.* Acupuncture (Niveau de preuve HAS : B)

### 3.6. British Columbia Cancer (BCA, Canada) 2014 🖲

Symptom Management Guidelines: xerostomia. BC Cancer Agency. 2014. [177971].

Acupuncture – Stimulation of salivary flow unclear, but may be helpful for some patients.

### 3.7. European Partnership for Action Against Cancer (EPAA, Europe) 2014 ⊕

Complementary and alternative medicine (CAM) in cancer care. Development and opportunities of Integrative Oncology. European Partnership for Action Against Cancer (EPAAC). 2014;:339P. [186081].

As to the use of acupuncture and TCM in the treatment of symptoms correlated to anti-cancer therapy, the literature has demonstrated a good level of evidence in the following cases: nausea and vomiting, pain, hotflashes and **xerostomia**, taking also in account the absence of relevant adverse effects and interactions.

# 3.8. Royal College of Surgeons of England / The British Society for Disability and Oral Health (RCSE, BSDOH, UK) 2012 $\oplus$

The Oral Management of Oncology Patients Requiring Radiotherapy, Chemotherapy and / or Bone Marrow Transplantation. Clinical Guidelines. The Royal College of Surgeons of England / The British Society for Disability and Oral Health. 2012:58p. [197604].

Acupuncture has minimal side effects and potential to increase salivary flow after radiotherapy where there is some residual function and is recommended. (IIB)

#### 3.9. Société Française d'Oto-Rhino-Laryngologie et de Chirurgie de la Face et

### du Cou (SFORL, France) 2014 ⊕

Recommandations pour la pratique clinique : Prise en charge des douleurs somatiques induites par les traitements des cancers des VADS. SFORL 2014 [160900].

*Recommandation 12:* Le groupe de travail recommande d'envisager l'acupuncture par un praticien expérimenté dans la prise en charge des douleurs cervicales séquellaires d'un curage ganglionnaire et dans la **xérostomie après radiothérapie**. (Grade B).

#### 3.10. American College of Chest Physicians (ACCP, USA) 2007 ⊕

Cassileth BR, Deng GE, Gomez JE, Johnstone PA, Kumar N, Vickers AJ; American College of Chest Physicians. Complementary therapies and integrative oncology in lung cancer: Accp Evidence-Based Clinical Practice Guidelines (2nd Edition). Chest. 2007;132(3sup:340s-54s. [146961]

*Recommendation 7.* Acupuncture is recommended as a complementary therapy when pain is poorly controlled or when side effects such as neuropathy or xerostomia from other modalities are clinically significant. Grade of recommendation, 1A

### 4. Randomized Controlled Trials

#### 4.1. Sources

- 1. **Acudoc2**: base de données du Centre de Documentation du GERA (ECR non inclus dans les revues systématiques sources).
- Mercadante 2017: Mercadante V, Al Hamad A, Lodi G, Porter S, Fedele S. Interventions for the management of radiotherapy-induced xerostomia and hyposalivation: A systematic review and meta-analysis. Oral Oncol. 2017;66:64-74. [10221].Garcia M, Niemtzow RC, McQuade J, Haddad R, Lee R, Spano M, Cohen L. Acupuncture for xerostomia in patients with cancer: An update. Medical Acupuncture. 2015; 27(3):158-67. [188884]
- 3. Lovelace 2014: Lovelace TL, Fox NF, Sood AJ, Nguyen SA, Day Ta. Management of radiotherapy-induced salivary hypofunction and consequent xerostomia in patients with oral or head and neck cancer: meta-analysis and literature review. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014. 117(5):595-607. [178881].
- 4. **Zhuang 2012**: Zhuang L, Yang Z, Zeng X, Zhua X, Chen Z, Liu L, Meng Z. The preventive and therapeutic effect of acupuncture for radiation-induced xerostomia in patients with head and neck cancer: a systematic review. Integr Cancer Ther. 2012. [159293].
- 5. **Jensen 2010**: Jensen SB et al. A systematic review of salivary gland hypofunction and xerostomia induced by cancer therapies: Management strategies and economic impact. Support Care Cancer. 2010; 18(8):1061-79. [155308].
- 6. **O'sullivan 2010**: O'Sullivan EM, Higginson IJ. Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review. Acupuncture in Medicine. 2010. 28(4):191-9.

#### 4.2. List

2019	Garcia MK, Meng Z, Rosenthal DI, Shen Y, Chambers M, Yang P, Wei Q, Hu C, Wu C, Bei W, Prinsloo S, Chiang J, Lopez G, Cohen L. Effect of True and Sham Acupuncture on Radiation-Induced Xerostomia Among Patients With Head and Neck Cancer: A Randomized Clinical Trial. JAMA Netw Opn. 2019;2(12):e1916910. [189899].	Acudoc2
2015	Wong RK, Deshmukh S, Wyatt G, Sagar S, Singh AK, Sultanem K, Nguyen- Tân PF, Yom SS, Cardinale J, Yao M, Hodson I, Matthiesen CL, Suh J, Thakrar H, Pugh SL, Berk L. Acupuncture-like transcutaneous electrical nerve stimulation versus pilocarpine in treating radiation-induced xerostomia: results of rtog 0537 phase 3 study. Int J Radiat Oncol Biol Phys. 2015;92:220-7. [179422].	Mercadante 2017
2012	Alimi D, Poulain P, Brulé S, Véricel R, Cornillot P, Le Toumelin P. Étude contrôlée randomisée évaluant l' action de l' auriculothérapie dans la xérostomie induite par la radiothérapie des tumeurs de la tête et du cou. Rev Odontostomatol. 2012;41:245-59. [202488].	Acudoc2
	Meng Z, Garcia MK, Hu C, Chiang J, Chambers M, Rosenthal DI, Peng H, Zhang Y, Zhao Q, Zhao G, Liu L, Spelman A, Palmer JL, Wei Q, Cohen L. Randomized controlled trial of acupuncture for prevention of radiation- induced xerostomia among patients with nasopharyngeal carcinoma. Cancer. 2012;118(13):3337-44. [168234].	Garcia 2015, Zhuang 2012
	Meng Z, Garcia KM, Hu C, Chiang J, Chambers M, Rosenthal DI, Peng H, WU C, Zhao Q, Zhao G, Liu L, Spelman A, Palmer L J, WEI Q, Cohen L. Sham- controlled, randomised, feasibility trial of acupuncture for prevention of radiation-induced xerostomia among patients with nasopharyngeal carcinoma. Eur J Cancer. 2012;48(11):1692-9. [166239]	Garcia 2015
	Simcock R, Fallowfield L, Monson K, Solis-Trapala I, Parlour L, Langridge C, et al. Arix: a randomised trial of acupuncture V oral care sessions in patients with chronic xerostomia following treatment of head and neck cancer. Ann Oncol. 2013;24(3):776-83. [157595].	Mercadante 2017, Garcia 2015
2010	Pfister DG, Cassileth BR, Deng GE, Yeung KS, Lee JS, Garrity D, Cronin A, Lee N, Kraus D, Shaha AR, Shah J, Vickers AJ. Acupuncture for pain and dysfunction after neck dissection: Results of a randomized controlled trial. J Clin Oncol. 2010;28(15):2565-70. [155389]	Garcia 2015, Zhuang 2012, O'sullivan 2010
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