

Systematic Review

Mandibular implant stability in oral cancer patients: a systematic review

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Abstract – Introduction: Dental implants have been increasingly used in cancer patients for dental rehabilitation of the previously irradiated mandible and in mandibular reconstruction *via* fibula grafts but there is still debate surrounding the osseointegration process of implants in both situations. Implant stability, measured with the resonance frequency analysis, can provide a better understanding of osseointegration. The objective of this systematic review was to assess the changes in the implant stability for dental implants over time in oral cancer patients and to determine whether the measurement of the Implant Stability Quotient at the time of implant placement could be a predictive factor of implant failure. **Materials and methods:** An electronic search of PubMed, ScienceDirect, and Google Scholar databases was performed prior to August 2023 and complemented by a manual search. The protocol of this systematic review was conducted in accordance with the PRISMA guidelines and registered in the International Prospective Register of Systematic Review (PROSPERO) database under number CRD42022378722. Studies reporting on dental implants, with measurement of the Implant Stability Quotient on mandibles, irradiated or not, with or without a fibula graft were included. **Results:** The search yielded 25 articles: 20 focused on native mandibles, 2 focused on irradiated mandibles and 3 focused on fibula grafts. The mean Implant Stability Quotient for native mandibles and fibula grafts was significantly higher than that for irradiated mandibles ($p < 0.05$). There was no significant difference in Implant Stability Quotient scores between native mandibles and fibula graft at any time point. A correlation between implant failure-Implant Stability Quotient could not be established due to a lack of available data in the relevant studies. **Discussion:** Notwithstanding the disparities in ISQ, the overall changes in ISQ over time in the three groups appeared to be homogeneous. The success rate of implants placed in the native mandible (97.38%) was found to be higher than that of implants placed in a fibula graft (94.59%) or irradiated mandible (87.2%). Despite the higher percentage of failures observed, the overall success rate confirming that dental implants are a reliable therapeutic option for cancer patient rehabilitation. **Conclusion:** Based on this review, it can be concluded that the change in the Implant Stability Quotient appeared to be comparable across all bone types. The mean Implant Stability Quotient in native mandibles and free fibula grafts was significantly higher than in irradiated mandibles. It was not possible to determine whether measuring the Implant Stability Quotient during implant insertion could predict implant failure.

Introduction

Over the past two decades, dental implants have been increasingly used in cancer patients for dental rehabilitation of the previously irradiated mandible and in mandibular reconstruction *via* fibula grafts. However, there is still debate surrounding the osseointegration process of implants in both situations [1].

Osseointegration is dependent on both primary stability, primarily mechanical, and secondary stability, primarily biological. When the implant is inserted into the jawbone, the biomechanical anchoring provides the foundation for

biological anchoring. An early inflammatory and vascular phase involving the mechanisms of healing and immunity precedes a phase of woven bone formation [2]. Bone maturation then continues until approximately 6 months after implant placement. The current consensus protocol in native mandible is to load the implant after 3 months of osseointegration [3].

Radiation therapy results in a reduction in the vascular portion of the target tissue and in decreased cellularity and hypoxia [4]. Osteoblast activity and consequently bone modeling and remodeling are impaired. Vascular density and vascular area fraction are lower in the irradiated bone than in the native mandible [5]. Consequently, the success rate of implants placed in an irradiated mandible (91.9%) is significantly lower than that of implants placed in a native mandible (97%) [6].

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Table I. Summary of scientific data on implant loading guided by Ostell (ISQ).

ISQ value	<60 (Low stability)	60–64 (Medium stability)	65–69 (Medium stability)	≥70 (High stability)
	2-stage, conventional loading, re-measure at follow-up > 2 months [11,12]	Full splint: 1-stage, immediate loading Partial case: 1-stage, immediate loading	Full splint: 1-stage, immediate loading Partial case: 1-stage, immediate loading	Full splint: 1-stage, immediate loading Partial case: 1-stage, immediate loading
	Consider conservative approach due to low implant stability (<i>i.e.</i> , relatively high implant mobility) [13]	Single case: 2-stage, conventional loading, re-measure at follow-up >2 months [11,12,14]	Single case: 1-stage, early loading, re-measure at follow-up 6–8 weeks [11,15,16]	Single case: 1-stage, immediate loading [11,15,17,18]

The fibula graft is currently regarded as the gold standard technique for mandibular reconstruction. The graft survival rate is reported to be as high as 95% [6]. The bi-cortical bone of the fibula graft has an outstanding capacity to receive dental implants resulting in a high success rate (93%–99%) [7].

Implant failure in irradiated bone can result in significant bone loss [8]. Moreover, bone alteration can lead to necrotic and exposed areas of bone that fail to heal within 3–6 months, without tumour recurrence, thus termed osteoradionecrosis (ORN). A 3% incidence of ORN has been reported in the literature following dental implant placement [6].

It is noteworthy that mechanical conditions may influence the success rate of implants, particularly in irradiated bone. Therefore, it is crucial to avoid a too-early loading of such implants. This may result in soft tissue inflammation, peri-implantitis, bone loss around the implant and implant mobility which could ultimately lead to ORN. Consequently, a lack of stability in the implant due to alterations in the bone caused by radiation may be indicative of an increased risk of implant failure, and even more so of a potential ORN.

To assess implant stability, a non-invasive and painless test method using resonance frequency analysis (RFA) has been proposed [9]. The Ostell® system (W&H, 1999) is based on a removable device, the Smartpeg®, screwed inside the implant. An electronic gauge records the stability of the implant on both sides (bucco-lingual and mesio-distal sides) and thus determines an implant stability quotient (ISQ), which ranges from 1 to 100, according to the peri-implant bone status. A higher ISQ value indicates greater implant stability, with an ISQ value over 70 considering an indicator of optimal implant stability [10]. ISQ monitoring over time provides a numerical representation of the evolution of implant stability. The ISQ scale can assist the practitioner in determining the optimal time for implant loading (Tab. I).

Other systems, *i.e.* Periostest®, measure the reaction of the periodontium to a defined percussive force and may be employed to assess implant stability. However, RFA has demonstrated greater reproducibility and predictability in assessing changes in bone-implant contact, with enhanced sensitivity to changes in implant stability [2,8,9].

Several factors have been identified as influencing [19] the accuracy of RFA monitoring. These include the spatial direction of the measurements, the patient's gender, the location of the

implant, the timing of implantation (immediate or delayed), the implant diameter and length, the insertion torque, the micro and macro design of the implant, the quality of the bone, the number of implants and the surgical protocol.

Our hypothesis was that the stability of dental implants, assessed by ISQ measurements, could serve as a predictive factor of implant failure in irradiated bone with or without fibula graft.

A systematic review of the literature was therefore conducted in accordance with the PRISMA methodology [20], with the following objectives: (1) to study the changes in the ISQ of dental implants over time in oral cancer patients (in previously irradiated mandibles or in mandibles reconstructed by fibula grafts) and in a control group (native mandible) and (2) to determine whether the ISQ measurement at the time of implant placement could be a predictive factor of implant failure.

Materials and methods

The protocol of this systematic review was conducted in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [20].

The protocol was registered in the PROSPERO database under number CRD42022378722.

Eligibility criteria

The PECO criteria [21] (population [P], exposure [E], comparison [C], outcome [O]) for this study were: (1) P – patients treated with dental implant(s) in an irradiated or non-irradiated mandible, with or without fibula graft reconstruction; (2) E – assessment of the ISQ at the time of implant placement and over time; (3) C – changes in ISQ values and number of implant failure(s) over time in irradiated or non-irradiated bone with or without a fibula graft; (4) O – to highlight a potential difference between the different sites of implantation (native mandible, irradiated mandible, fibula graft) and a potential correlation between changes in the ISQ value and implant failure.

In accordance with the Pisa Consensus Conference, a consensus statement endorsed by the International Congress of Oral Implantologists, implant failure is defined as: any pain, vertical mobility, or uncontrolled progressive bone loss that necessitates implant removal [22].

The inclusion criteria were the following: (1) clinical trials (randomized or not); (2) articles available in French and English; (3) implantation in mandibular bone irradiated or not irradiated with or without fibula graft reconstruction; (4) implantation in completely healed alveolar socket after tooth extraction and (5) evaluation of implant stability with the ISQ.

Studies with the following characteristics were not included: (1) isolated case reports, meta-analyses and literature reviews (narrative, comprehensive, systematic); (2) animal experimental studies; (3) implantation in other facial bone (maxilla, zygoma, craniofacial implants) or in other grafts than fibula (auto-, allo-, xeno-grafts, biomaterials); (3) immediate loading of implants, extraction/implantation at the same time (immediate placement); (4) no report of ISQ or no ISQ follow-up ; and (5) full text unavailable.

Information sources and search strategy

The literature search was performed on Pubmed, Science Direct and Google Scholar, with all articles published before August 2023 being included. Additionally, a manual search of the reference lists of the selected articles was performed.

The search was performed with the following MeSH term combinations: “mandible”, “irradiated mandible”, “fibula flap”, “dental implant”, “ISQ,” “implant stability quotient”, “RFA”, “resonance frequency analysis.”

To illustrate, the equation search for PubMed was as follows: ((“mandible”[TW] OR “irradiated mandible”[TW] OR “fibula flap”[TW]) AND (“dental implant”[TW] OR “dental implants”[TW]) AND (“ISQ”[TW] OR “Resonance frequency analysis”[TW] OR “RFA”[TW]) AND (1990/12/12:3000[dp])).

Selection process

After removing duplicates resulting from the search, the first selection round was made by two independent reviewers who read the titles and abstracts. Then, after reading the full text, a second selection was performed by two independent reviewers. In cases of disagreement, a third reviewer was involved.

Data collection process

Data extraction was independently performed by two reviewers. The data were extracted using an Excel data collection form. Data were collected on the following: title and characteristics of the study; number of patients; type of bone; irradiation dose; number and characteristics of the implants (brand, diameter, length); ISQ value over time and time interval for ISQ measurements; implant failure (and related ISQ value) and potential correlation with implant failure.

Data analyses

Reviewers gathered ISQ measures and implant success rates in a spreadsheet (Microsoft Excel) from the selected studies to calculate the mean, median, and their standard deviations in subgroups (native mandible, irradiated mandible and fibula graft).

The mean and standard deviation (SD) were employed to compare the ISQ with graphics in the native mandible, irradiated mandible and fibula flap groups. A Student *t* test was used for comparison. A *p* value less than 0.05 was deemed to indicate a statistically significant result.

Subgroup analyses were performed depending on the type of bone *i.e.*, native mandible, irradiated mandible, and fibula flap.

Assessing the risk of bias and the quality of studies

The risk of bias and quality of each study were assessed depending on the type of study according to the Risk Of Bias In Non-randomized Studies — of Intervention (ROBINS-I) tool [23], the Cochrane risk of bias tool for randomized trials (RoB 2) [24] and the CEBM Oxford level of evidence classification [25]. Disagreements between the two investigators were resolved by a third reviewer (AC).

The risk of bias was classified as follows: red = high risk of bias; orange = moderate risk of bias; green = low risk of bias; white = not applicable.

Results

Study selection

A total of 469 articles were screened (234 from PubMed, 41 from Google Scholar, 194 from Science Direct) of which 6 duplicates were removed (Fig. 1).

On the 463 remaining articles, 399 were excluded following a screening of the titles and abstracts: 110 articles investigated immediate loading; 39 articles used other bone grafting than fibula grafts; 28 articles were devoted to maxillary bone; 35 articles studied implants in cadavers; 15 articles had insufficient content; 10 articles studied extra-oral or zygomatic implants; 6 articles were isolated case reports; systematic reviews or meta-analyses; and 156 articles were off topic.

Of the 64 remaining articles, 39 were excluded following a full-text reading because 21 of these articles did not mention ISQ measures, while 18 did not report on ISQ follow-up.

Finally, 25 articles that met all the inclusion criteria were included in this systematic review.

Characteristics of included studies

A total of 1830 implants and 505 patients were included in the 25 selected articles. One article did not specify the number of implants utilized [26] and eight articles did not specify the number of patients who underwent implantation [26–33].

These studies were carried out in different countries, with no specific location identified, the characteristics of the studies are presented in Table II.

Overall, 20 studies investigated an ISQ follow-up in mandibular non-irradiated bone, two in the irradiated mandible and three in a reconstructed mandible with a fibula graft.

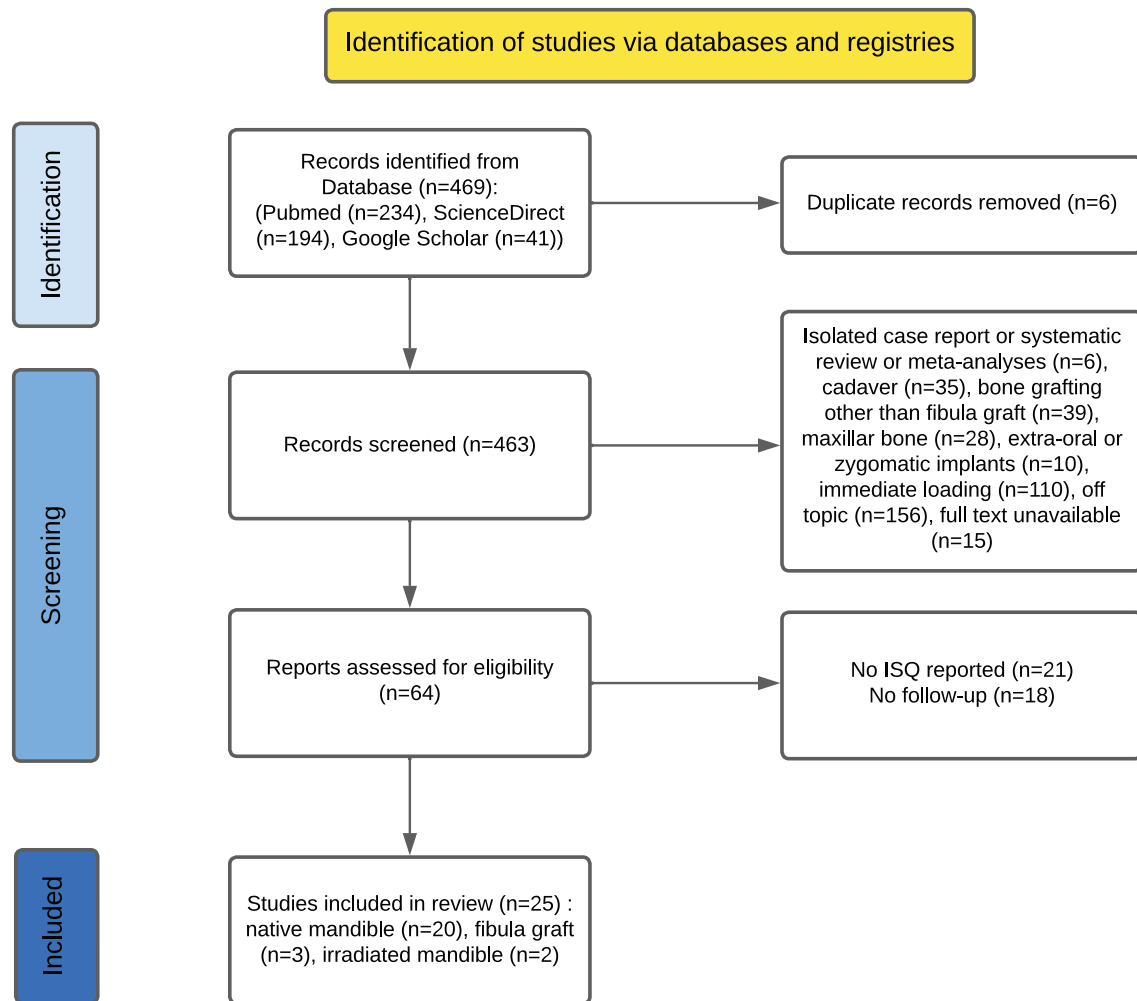


Fig. 1. Study flow-chart.

Native mandible

Of the 20 studies regarding native mandibles, 18 were prospective and 2 were retrospective. Publication years ranged from 2012 to 2022. A total of 1380 implants were placed, while one study did not specify the number of implants [26].

A total of seven different implant systems were used: Straumann® (7 studies [27,28,31,33–36], De Bortoli® (1 study [29]), MG-Osseous® (1 study [37]), Neodent® (2 studies [38,39]), Signo® (1 study [32]), Zimmer® (1 study [40]), Dentsply® (1 study [41]), one study used both Astra® and Straumann® implants [42] and four studies did not specify the implant system [26,43–45]. The implant lengths ranged from 4 to 16 mm with diameters varying from 2.9 to 5 mm.

Regarding the ISQ, the monitoring duration was as follows: 6-weeks for three studies [28,30,39], 7-weeks for one study [31], 2-months for one study [27], 11-weeks for one study [34], 3-months for six studies [32,35,41–43,45], 4-months for one study [37], 5-months for one study [29], 1-year for four studies [26,36,38,40], and 2-years for one study [44].

Irradiated mandible

In studies involving irradiated mandibles, the two selected articles were published in 2011 [46], and in 2015 [47].

Overall, two prospective studies were included; 205 implants were placed in the irradiated mandibles.

One study used Straumann® [47], while the other used a combination of Astra®, Nobel® and 3i® [46]. The lengths of the implants ranged from 10 to 13mm, with no specification of the diameter.

One study [46] reported a radiation dose ranging from 50 to 70-Gy, while the second study did not report the radiation dose.

One study recorded the ISQ over a 5-month period [46] while the other study recorded it over a 1-year period [47].

Fibula graft

For studies involving fibula grafts, publication years ranged from 2005 to 2020.

Table II. Main characteristics and results of the included studies. grey cells: missing data; black cells: data not relevant. N°: number; ISQ°: implant stability quotient; SD : standart deviation; Ø°: diameter; W°: weeks; M°: months; Y°: year.

Selected study (first author and publication year)	Type of study	Patients (n)	Type of bone	Implants (n, characteristics)	ISQ + SD	Implant failure, remark	Radiation dose
Bafjari (2019)	Prospective	42	Native mandible	77	D0= 63.81±9.48, M3= 70.25±9.3	0	
Faot (2019)	Prospective	31	Native mandible	62 Neodent®: Ø 2.9-10mm		12	
García (2011)	Prospective	70	Native mandible	68 MG-Osseous®: Ø 3.75-4.25mm	D0=79.6±5.4, D110=77.45±5.6	2, decrease of more than 10 ISQ points was observed in RFA between first and second surgical stages.	
Gehrke (2014)	Prospective		Native mandible	41 De Bortoli® Ø 3.5-5mm Length 8-13mm	D0=65.5, M3=72.9, M5=75.3	0	
Guirado (2015)	Prospective	10	Native mandible	60 Straumann® Length 4-10 mm	Shorts: D0=75.22±1.23, M3=78.33±1.76, M6=79.65±0.56, M12=80.20±0.44 Conventional: S0=78.72±2.13, M3=81.67±1.22, M6=82.45±0.78, M12=82.34±0.67 D0= 65.9±8, M1= 64.4±7.6, M2= 72.1±5.5	1	
Guler (2013)	Prospective		Native mandible	95 Straumann® Ø 3.3-4.8mm Length 8-14 mm	Astra® D0=77.8±6.1, M3=78.9±7.8, Straumann® D0=66.5±16.5, M3=73.9±8.4	0	
Hadzik (2017)	Prospective	13	Native mandible	16 shorts Astra® (OsseoSpeed TX Bone Level)		0	
Hakobyan (2020)	Prospective	27	Fibula graft	16 shorts Straumann® (SLActive, Tissue level)	D0 = 65, M3=73	7	0 Gy
Karl (2008)	Retrospective		Native mandible	226 Straumann®: Ø 3.3-4.8mm, Length 6-16mm	Anterior mandible (n=65): D0=71.92±7.8, S7=76.84±4.9 Posterior mandible (n=161): D0=75.98±5.9, S7= 79.45±4 D0 = 75.3, W6= 76.96	0	
Krafft (2015)	Prospective		Native mandible	264 Straumann®: Ø 3.3-4.8mm Length 6-14mm		<8	
Kramer (2005)	Prospective	16	Fibula flap		D0= 70.1, M3= 71.4, M12=76	3	0 Gy

Table II. (continued).

Selected study (first author and publication year)	Type of study	Patients (n)	Type of bone	Implants (n, characteristics)	ISQ + SD	Implant failure, remark	Radiation dose
Makary (2012)	Prospective		Native mandible	51 Ø 3.75mm Length: 10-15mm	D0=82, W3=78, W6 =78	0	
Mei (2022)	Prospective		Native mandible	40 Zimmer®; Ø 4.1-4.7mm 32 Straumann®; Ø 4.1-4.8mm	Osteotome: D0=70.75±4.28, W1=72.39±3.99, W2=72.55±4.62, W3=72.87 +/−2.9, W4=74.05 +/− 2.91, W6=75.77+/−1.97, W8=76.47±2.52, W10 =76.83±2.78, W12=77.5±3.09 Conventional: D0=78.33±6.63, W1=76.74±7.76, W2=74.26±6.34, W3=76.52±6.34, W4=77.09±6.39, W6=77.57±5.32, S8= 78.48±4.77, W10=78.33±4.55, W12=78.68±4.51 D0=79.48±2.35, W20=75.59±5.11 D0: C(Control) = 75.7 SD 5.6, L (Laser) = 77.4 SD 3.4 D10: C = 76.2±4.6, L = 78.9±3.7 W3: C = 76.9±3.5, L = 76.8±4.6 W6: C = 76.3±2.3, L = 75.5±4.0 W9: C = 77.7±3.5, L = 76.2±4.9 W12: C = 78.4±3.0, L = 76.3±4.1 D0=67.35±6.67, Y2=72.91±5.07	0	
Möhlhenrich (2016)	Prospective	25	Fibula graft	50 Straumann®			7 patients
Morales (2012)	Prospective	8	Native mandible	30 Dentsply®		0	
Pieri (2012)	Prospective	25	Native mandible	61		2	
Queiroz (2015)	Prospective	23	Native mandible	48 shorts: Ø 5mm Length 5.5-7 mm; 42 regular: Ø 4mm Length 10-11.5 mm	D0: S(short) = 71; C (conventional) = 63, W2 S = 68, C =65, M1 S = 71, C = 70, M2 S = 69, C= 71, M3 S = 70, C = 70 Native: D0= 68.4±9.6, W1= 60.05±6.9, W2=59.05±6.3 M3 (loading)= 67.95±6.6, M4= 62.15±6.1, M6= 70.7±7.3, Y1 = 75.75±6.5 Irradiated: D0= 62.4±7, W1= 52.1±5, W2=49.25±3.3,	Survival rate (90 days) 87.5% for shorts and 100% for regular	
Saracoglu (2015)	Prospective	40	Native and irradiated mandible	80 Straumann®			

Table II. (continued).

Selected study (first author and publication year)	Type of study	Patients (n)	Type of bone	Implants (n, characteristics)	ISQ + SD	Implant failure, remark	Radiation dose
Shokri (2013)	Prospective	10	Native mandible	15 Straumann®	M3 (loading)=59.65±6.4, M4: 55±3.7, M6 = 63.65±5.7, Y1= 67.3±7.1 D0= 77.20±4.92, W1=77.00±3.51, W2= 74.20±3.82, W3= 73.20±5.19, W4=72.13±5.69, W5= 72.33±4.62, W7= 73.55±3.89, W11=75.60±3.72 D0= 69.75, M6 = 69.05, Y1= 71.7	0	
Sreerama (2021)	Prospective		Native mandible			<15 RFA=65.4±5.8 in successful implants and 45.8±4.1 in failed implants	50-70 Gy
Store (2011)	Prospective	31	Irradiated mandible	125: Astra® ,Straumann®, 3i®, Nobel® ø 4.1-4.5mm Length 10-15mm			
Sun (2016)	Prospective	32	Native mandible	45 Straumann®: RN ø 4.8 Length 10 mm	Smokers: D0=82, W1=76, W2=72, W3=72, W4=74, W6=76, W8=78, W12=80 No smokers: D0=78, W1=76, W2=68, W3=76, W4=78, W6=80, W8=81, W12=82 D0=68±2.5, M12=71.77±2.01	0	
Tözüm (2016)	Prospective	82	Native mandible	82 Zimmer®: ø 3.75-4.7mm, Length 8-13 mm			
Velloso (2019)	Prospective	20	Native mandible	20 Néodent®: ø 3.75mm Length 11mm	Hydrophilic: D0=62.7±8.6, W1=65.1±5.9, W2=64.9±8.3, W3=65.9±6.6, W4=66.3±5.5, W5=66.9±5.8, W6=67.1±5.9 Control: W0=63.5±8.4, W1=62.9±8.9, W2=59.2±8.6, W3=58.5±8.1, W4=59.1±7.7, W5=60.4±7.4, W6=61±7.2 D0: Tapered (67.86±12.28) cylindrical (62.62±16.99) W1: Tapered (53.97±17.86) cylindrical(59.54±14.55) W2: Tapered (69.29±13.55) cylindrical (67.65±15.47) W3: Tapered (77.58±9.59) cylindrical (77.96±8.12)	0	
Waechter (2017)	Prospective		Native mandible	40 Signo®: 20 tapered: ø 4.60 mm 20 cylindrical: ø 4mm Length 10 mm		3	

Table II. (continued).

Selected study (first author and publication year)	Type of study	Patients (n)	Type of bone	Implants (n, characteristics)	ISQ + SD	Implant failure, remark	Radiation dose
					W6: Tapered (71.19±9.67) cylindrical (71.90±12.84) W10: Tapered (73.58±8.58) cylindrical (70.87±7.94) M3: Tapered (78.61±8.85) cylindrical (79.62±8.52)		

A total of three prospective studies were selected for inclusion representing 235 implants placed.

Two studies did not specify the type and brand of implant used [48,49], while one study employed Straumann® [50]. Implant lengths ranged from 10 to 15mm and the diameters were not specified.

Both irradiated and non-irradiated fibula grafts were reported [50] reported on seven irradiated patients out of 26 but did not provide the number of implants in case of irradiated fibula grafts. Furthermore, the radiation doses were not reported, and no comparison between irradiated and non-irradiated patients was available. The studies conducted by Kramer and Hakyoban [48,49] were exclusively focused on non-irradiated fibula grafts.

One study recorded the ISQ for a period of 3 months [49], another for a period of 5-months [50], and one for a period of 1-year [48].

Results of the included studies

Follow-up of the mean ISQ

The mean ISQ and standard deviation (SD) for the native mandible, irradiated mandible and fibula graft are shown in Figure 2.

These values were reported at 16 different time points for the native mandible: On the day of surgery (D0), then at weekly intervals for 12-weeks (W1-W12), and on the 16th, 21st, 24th and 48th weeks (W16, W21, W24 and W48).

The data for implants placed in the irradiated mandible were collected at seven different time points: D0, W1, W2, W12, W16, W24 and W48.

The implant stability of fibula grafts was evaluated at four distinct time points: D0, W12, W21 and W48.

Native mandible

The mean ISQ in the native mandible group decreased during the first 2-weeks (D0: 71 (62.4–82) to W2: 64.2 (49.3–74.3)), between the fourth and the fifth weeks (W4: 69.1 (62.7–77.1) to W5: 66.5 (63.1–72.3)), and between the 11th and 16th weeks (W11: 77.4 (75.6–79.1) to W16: 63.8 (55–77.5)).

The mean ISQ increased for the third week (W3: 72.5 (62.2–78)), between the fifth and sixth weeks (W5: 66.5 (63.7–72.3) to W6: 75.1 (64.1–78)), between the 16th and the 21st weeks (W16: 63.8 (55–77.5) to W21: 75.3) and between the 21th and 48th weeks (W21: 75.3 to W48: 75.1 (67.3D82.3)).

The mean ISQ remained consistent between the sixth and 11th weeks (W6: 75.1 (64.1–78) to W11: 77.4 (75.6–79.1)).

Irradiated mandible

In the case of the irradiated mandible group, the mean ISQ was observed to decrease during the first 2-weeks (D0: 62.4 to W2: 49.25), and between the 12th and the 16th weeks (W12 (59.65) to W16 (55)). The mean ISQ exhibited an upward trend between the 24th and the 48th weeks (W24: 63.6 to W48: 67.3).

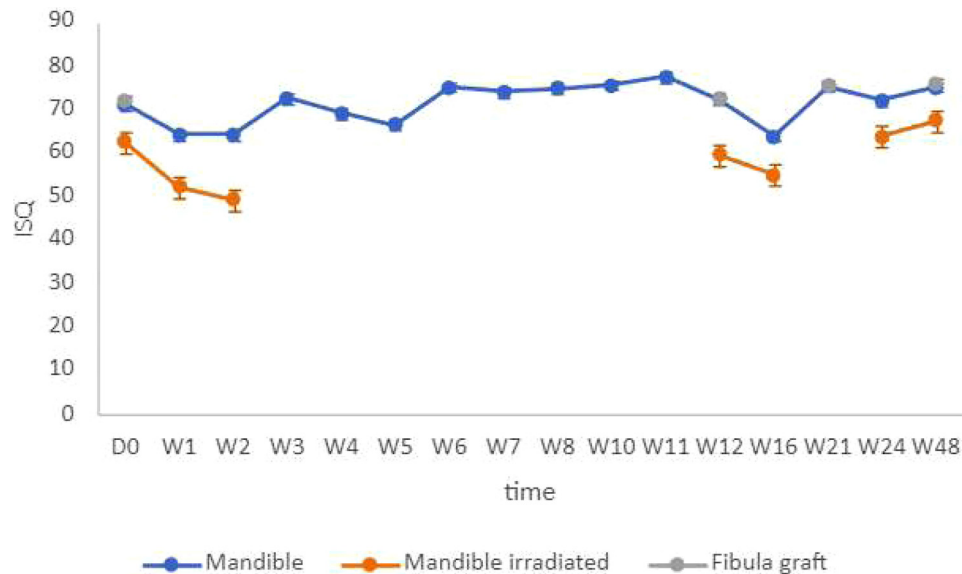


Fig. 2. Changes in the mean ISQ+SD over time for native mandibles (blue), irradiated mandibles (orange), and fibula grafts (gray).

Fibula graft

The mean ISQ of the fibula graft group at each recorded time point (D0: 72 (65–79.5), W12: 72.2 (71.4–73), W21: 75.6 and W48: 76) overlapped with that of the native mandible group.

At any time that it was recorded, the mean ISQ for the native mandible and the fibula graft groups was significantly higher ($p < 0.05$) than that for the irradiated mandible group. But no significant difference was reported regarding ISQ values between native mandible and fibula graft at any time ($p < 0.05$).

No correlation between radiation dose and ISQ could be established due to the lack of available data. One of the two studies did not provide any information on the radiation dose [47]. For the irradiated mandible and for the fibula graft groups, two studies did not include irradiated patients [48,49] and one [50] indicated that 7 out of 26 patients underwent radiotherapy, but the ISQ of the patients who benefited from radiotherapy was confounded with the ISQ of patients who did not, thus preventing any conclusion being drawn.

Implant failure

In the native mandible group, 34 of 1298 implants were lost, *i.e.*, 2.62%. One of the 21 selected studies did not report implant failures [40].

In the irradiated mandible group, 16 of 125 implants (12.8%) were lost, with 9 losses being due to ORN (7.2%). One study did not present data on implant failures [47].

In the fibula graft group, the implant failure rate was 5.41%, with 10 losses out of 185 implants. One of the three studies did not report implant failures [50], and no case of ORN was reported.

The success rate of dental implants was found to be lower in irradiated mandibles than in fibula grafts, which in turn exhibited a lower success rate than native mandibles. However, these observations must be regarded as preliminary, given that no statistical test could be performed due to the limited number of implants inserted in irradiated mandible or in fibula graft in the selected studies.

It was not possible to correlate ISQ values with implant failure as the ISQ values of the lost implants were not precisely stated in the relevant studies.

A comparison of implant-related ORN rates in irradiated mandibles and in fibula grafts was not possible due to the lack of data and the heterogeneity of the dedicated studies.

Assessment of biases

In accordance with the OCEBM scale, no study achieved a level of evidence greater than to 3. In total, 23 studies were classified as presenting a level of evidence of 3 while two studies were classified as presenting a level of evidence of 4.

The results of the evaluation of bias are listed in Table III.

Discussion

The objective of this systematic review was twofold: (1) to examine the changes in the ISQ of dental implants in oral cancer patients with previously irradiated mandibles or in mandibles reconstructed by fibula grafts in comparison, with a control (group comprising native mandibles) and (2) to ascertain whether the measurement of ISQ at the time of implant placement could be a predictive factor of implant failure.

Table III. Analysis of risk of bias and level of evidence according to the ROBINS-I, the RoB 2.0, and CEBM Oxford level of evidence classification. Red: high risk of bias, orange: moderate risk of bias, green: low risk of bias, white: not applicable.

	Bias due to confounding	Bias arising from measurement of the exposure	Bias in selection of participation	Bias due to post-exposure intervention	Bias due to missing data	Bias arising from measurement of the outcome	Bias in selection of the reported result	Level of evidence
Bafjari 2019	Orange	Orange	White	White	Orange	Orange	Green	3
Faot 2019	Green	Green	White	White	Green	Red	Green	3
García 2011	Green	Green	White	White	Green	Red	Green	3
Gehrke 2014	Green	Green	Green	White	Green	Orange	Green	3
Guirado 2015	Green	Green	White	White	Green	Red	Green	3
Guler 2013	Green	Green	White	White	Red	Red	Green	3
Hadzik 2017	Green	Green	White	White	Green	Red	Green	3
Hakobyan 2020	Red	Green	White	White	Green	Red	Green	3
Karl 2008	Red	Green	Green	White	Green	Red	Green	3
Krafft 2015	Orange	Orange	Green	White	Green	Red	Green	3
Kramer 2005	Orange	Green	White	White	Green	Orange	Green	3
Makary 2012	Orange	Green	White	White	Green	Red	Green	3
Mei 2022	Green	Green	Green	White	Green	Red	Green	3
Möhlhenrich 2016	Red	Green	Green	White	Green	Red	Green	3
Morales 2012	Green	Green	Green	White	Green	Red	Green	3
Pieri 2012	Green	Green	White	White	Red	Red	Green	3
Queiroz 2015	Green	Green	Green	White	Green	Red	Green	3
Saracoglu 2015	Green	Green	Green	White	Green	Red	Green	3
Shokri 2013	Green	Green	White	White	Green	Red	Green	4
Sreerama 2021	Orange	Green	White	White	Green	Red	Green	3
Støre 2011	Green	Green	Green	White	Green	Red	Green	3
Sun 2016	Green	Green	Green	White	Green	Green	Green	3
Tözüm 2016	Green	Green	White	White	Green	Red	Green	3
Velloso 2019	Green	Green	Green	White	Green	Red	Green	4
Waechter 2017	Green	Green	Green	White	Green	Red	Green	3

This systematic review revealed that implants placed in a native mandible and a fibula graft exhibited a significantly higher ISQ than those placed in an irradiated mandible.

These findings align with those of Saracoglu [47], who similarly observed a tendency towards reduced ISQ values in irradiated mandibles relative to native mandibles. This may be explained by the effects of radiotherapy on the jawbone. Indeed, irradiation has been demonstrated to reduce cortical volume and increase bone porosity around the implant, with focal necrosis and fibrosis [51]; this compromises the biomechanical properties of bone around dental implants which are a pivotal determinant of implant stability [19].

It was found that there was no significant difference in the ISQ between the native mandible and the fibula graft groups. Nevertheless, the overall changes in ISQ over time in the three groups appears to be relatively homogeneous. The decrease in ISQ values recorded in all groups during the initial 2-week period following implantation may be indicative of the initial

inflammatory phase of bone remodeling [52]. In the native mandible group, the subsequent increase in ISQ reaching a plateau from the sixth week post-implantation correlates with the conclusion of the initial phase of bone remodeling and the beginning of bone mineralization. The brief decline in ISQ observed between 12th- and 16th post-implantation weeks may be attributed to the loading of the implants as the bone surrounding them undergoes intensive remodeling.

Some studies [43,48] demonstrated a slight increase in the ISQ over time for implants placed in fibula grafts. This can be attributed to the bi-cortical anchorage of the implant in the thick cortical bone of the fibula graft. The absence of a difference in ISQ values between the fibula and the native mandible may also be attributed to these anatomical characteristics.

In experimental studies, the administration of radiotherapy has been observed to delay the bone healing process and lead to a reduction in bone quality and bone mineral density [52].

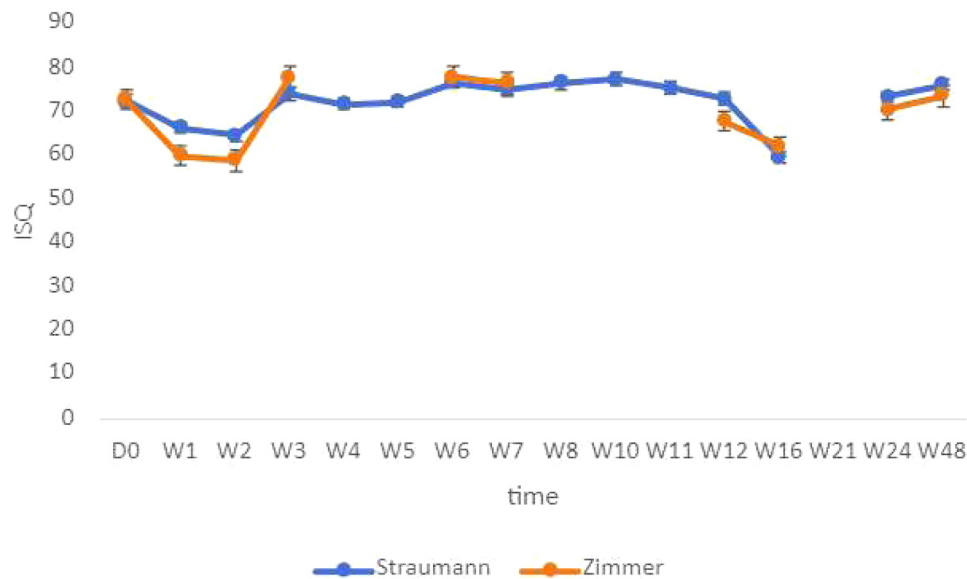


Fig. 3. Temporal assessment of the mean ISQ (+SD) for the Zimmer® and Straumann® implants in the native mandible.

Therefore, with this information it could be expected that the curve would shift to the right for the ISQ values of the irradiated mandible compared with the native mandible group. As illustrated in Figure 3, no such shift was observed, as the curves remained parallel and suggest a similar trend in implant stability. Nonetheless, the average ISQ values for the irradiated mandible remained lower than for the native mandible group. However, for the native mandible, the current consensus protocol is to load the implant after 12-weeks of osseointegration [3]. At this time, the mean ISQ for native mandible and fibula graft are respectively 72.4 and 72.2, considered to high stability (Tab. I) which means that the implant can be loaded. At 12-weeks, ISQ for irradiated mandible is 60, considered to medium stability (Tab. I). Despite a lack of data subsequent to the 16th week, if the curves remain parallel, as observed at other times between the native mandible, fibula flap and irradiated mandible groups, it can be hypothesized that the ISQ for the irradiated mandible exhibits significant increase between the 16th and 21st week, subsequently reaching a plateau phase until the 48th week. Consequently, it can be deduced that the ideal prosthetic loading time is achieved after 21 weeks of healing following the placement of a dental implant in an irradiated mandibular bone.

There is no consensus in the literature concerning the threshold dose of radiation that may affect the survival of dental implants [53,54]. Several authors have observed improved implant survival with low-dose radiation (<55 Gy) [54–56] and a systematic review reported that an average radiation dose of more than 60-Gy did not appear to have a negative impact on implant survival [6]. It is frequently reported that a high radiation dose is associated with an increased risk of implant failure and the onset of ORN, and the risk and severity of ORN are influenced by factors beyond the radiation dose including the dental health and oral hygiene of the patients [57].

However, the lack of data regarding radiation dose, particularly for failed implants, precludes analysis of this crucial point in our systematic review. A single study [46] provided data on the radiation dose delivered to the irradiated mandible, and two studies dealt with fibula grafts with no irradiation while one study did not specify the exact irradiation dose. In future studies, the use of software that offers precise knowledge of the radiation dose at the site of implantation, such as Dentalmaps® or Dero®, could provide more accurate data.

In this review, the success rate of implants placed in the native mandible (97.38%) was found to be higher than that of implants placed in a fibula graft (94.59%) or irradiated mandible (87.2%). Despite the higher percentage of failures observed in implants placed in irradiated mandibles, the overall success rate reached 87.2% confirming that dental implants are a reliable therapeutic option for irradiated patient rehabilitation.

In the literature, similar implant failure rates are reported for the native mandible and the fibula graft but not for the irradiated mandible (12.8% in our review *versus* 8.1% in the literature) [6,15]. This discrepancy may be due to the limited number of implants placed in the irradiated mandible within the scope of our review (205 implants) or to the elevated radiation dosage (125 implants were placed in bone that received a radiation dose between 50 and 70 Gy). Furthermore, some patients who experienced implant failure were smokers and tobacco use has been well documented as a risk factor for implant failure [35].

The sensitivity of RFA for monitoring changes in implant stability has been well documented in the literature [2,15,18,26]. Sreerama [26] compared the mean ISQ between successful implants and failed implants in native mandibles and reported that the ISQ for successful implants was significantly

higher than for failed implants ($p < 0.05$). Moreover, the ISQ value at implant placement for predicting implant failure could not be determined, as the sole study [46] attempting to reach a conclusion on this crucial point reported that the failing implants displayed very different ISQ values and not enough data to conclude that the ISQ value at the time of placement could serve as an indicator of the level of risk for implant failure.

However, the changes in the ISQ may inform the practitioner of the risk of implant failure. Studies conducted by García [37] and by Sreerama [26] indicated that a decline in the ISQ exceeding 10–20 was observed in implants that were ultimately unsuccessful. This implies that the ISQ could be indicative of peri-implant bone health.

However, there is currently no consensus regarding the optimal duration of the interval between successive measurements in order to make the ISQ a predictive criterion of implant failure and to use it in the routine follow-up of patients with implant rehabilitation. The Ostell® protocol recommends the ISQ be measured at implant placement for a baseline reading and then before loading without any time specified. It is not currently recommended that implant stability be routinely checked once the patient has been rehabilitated, but it would be beneficial for the practitioner to monitor this in order to prevent any failure. However, repeated measurement during the bone healing period after implantation may have a detrimental impact on dental implant osseointegration, as the practitioner is required to unscrew the implant abutment to perform such measurements at each interval [58]. Therefore, it is crucial to limit the number of unscrewing procedures and to provide comprehensive relevant guidelines regarding the current use of this device.

A correlation between radiation dose and ISQ (at the time of implantation, healing or loading) could not be established in this systematic review due to the lack of studies that directly compared the two variables in both successful and unsuccessful implant cases. Therefore, further research is required to gain a deeper understanding of the range of factors that may contribute to implant instability following radiotherapy.

Regarding the radiation dose, data on the time interval between irradiation and dental implantation were lacking in most of the studies. Most publications concur that a 12-month interval [6,56] should elapse between the conclusion of irradiation and the placement of the implant. A shorter time interval between irradiation and dental implantation appears to increase the risk of implant failure or ORN onset. With regard to implants placed in fibula flaps, a distinction was not made between primary implantation (concomitant to the graft) and secondary implantation which could also influence the success rate of the implants [6]. The interval between the end of irradiation and implant placement was also not reported. It is well documented that if an implant is loaded too early, this can lead to peri-implant bone loss and even to ORN in irradiated mandibles [58].

In this review, eight different implant systems were used (six studies did not report the implant system used [26, 43–45,48,49]). A variety of designs are used for implant systems with differing insertion protocols and torques which can result in

varying primary stability or bone stress [19]. We sought to compare the mean ISQ in native mandibles between the implant brands with the largest number of implants (Fig. 3). To achieve this, we compared the Straumann® brand which represented 737 implants, and the Zimmer® brand which represented 122 implants. Our findings indicated that the average ISQ curves exhibited similar variations. However, the curves were not overlaid, and there was a significant difference ($p < 0.05$) between the two brand particularly during the initial 3-weeks. When examining the manufacturer recommendations regarding the primary insertion torque to be respected, Straumann® asks that a primary insertion torque of 35-N.cm be respected for these implants, in contrast to insertion torques of 20–35-Ncm for Zimmer®. The manufacturer recommendations vary, and this can lead to heterogeneous RFA values, making comparisons between the eight different systems unreliable. To ensure the validity of such a comparison, it would be preferable to limit the number of implant systems used and to standardize the surgical placement procedures. Furthermore, it would be beneficial to report the insertion torque of each implant allowing for a potential correlation between the insertion torque and the initial ISQ value.

The studies selected for this systematic review were heterogeneous and sparse, thus limiting relevant comparisons and allowing for different interpretations. Significantly, very different procedures for implant insertion were used. Moreover, too few data on dental implants in irradiated bone or on fibula grafts are currently available for the moment. Furthermore, jawbone type, which is a crucial factor for initial bone stability was poorly investigated. Additionally, the three groups were widely imbalanced in terms of number of implants: from a total of 1380 implants, 1298 were placed in native mandibles, 205 in irradiated mandibles and 235 in fibula grafts. This may potentially lead to selection bias.

Additionally, other confounding factors may influence the results. For example, in one study [41], low-level laser therapy (LLLT) was introduced as an adjuvant therapy to enhance implant stability with conflicting results reported.

Thus, due to the heterogeneity and paucity of results, a meta-analysis was not possible.

Finally, most of the selected studies for this systematic literature review had a medium to low level of evidence.

Conclusion

Despite the limitations of this systematic review, some crucial information has been highlighted. The evolution of the ISQ during the primary stability interval appears to be comparable in all bone types, with or without radiotherapy. The mean ISQ in native mandibles and fibula graft was significantly higher than the mean ISQ in irradiated mandibles. It was not possible to identify a potential influence of the ISQ on implant loading; or to determine whether the measurement of the ISQ during implant insertion could predict implant failure; and thus prevent a potential implant-induced ORN.

A prospective clinical study is therefore required, using the same implant protocol, with a limited number of implant systems to record relevant data about torque insertion and to compare ISQ values in non-irradiated and irradiated mandibles with or without a fibula graft.

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Conflicts of interest

The authors declare no conflicts of interest in regards to this article.

Data availability statement

The data that support the findings of this study are available from the corresponding author [DB], upon reasonable request.

Author contributions statement

Author 1: Conceptualization, methodology, software, validation, formal analysis, investigation, resources, data curation, writing — original draft, writing — review & editing, visualization. **Author 2:** Writing — review & editing, visualization, project administration.

Author 3: Writing — review & editing, visualization, project administration. **Author 4:** Conceptualization, methodology, validation, investigation, resources, writing — original draft, writing — review & editing, visualization, supervision, project administration.

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