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Considerations preliminary to the application of early and immediate loading protocols in dental implantology

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In oral implantology, a 3–6 month stress-free healing period is presently accepted as a prerequisite to achieve bone apposition without interposition of a fibrous scar tissue. This protocol was introduced by Brånemark and co-workers in 1977. The aim of the present paper is to review the reasons that led Brånemark and collaborators to require long delayed loading periods. It is shown that the requirement for long delayed loading periods was drawn from the initiation and development periods of their original clinical trial. Demanding conditions were met involving simultaneously: 1) patients with poor bone quality and quantity, 2) non-optimized implant design, 3) short implants, 4) non-optimized surgical placement, 5) non-optimized surgical protocol and 6) biomechanically non-optimized prosthesis. Extrapolation of the requirement for long healing periods from these particular conditions to more standard situations involving refined surgical protocols and careful patient selection might be questioned. Albeit premature loading has been interpreted as inducing fibrous tissue interposition, immediate loading *per se* is not responsible for fibrous encapsulation. It is the excess of micromotion during the healing phase that interferes with bone repair. A threshold of tolerated micromotion exists, that is somewhere between 50 μm and 150 μm. It is suggested that loading protocols might be shortened through 2 different approaches. The first way would be to decrease stepwise the delayed loading period for free-standing implants below the presently accepted 3–6 months of healing. The second way would be to identify immediate loading protocols that are capable of keeping the amount of micromotion beneath the threshold of deleterious micromotion. Immediate loading protocols for implants-retained overdentures and fixed bridges are reviewed. It is shown that successful premature loading protocols require a careful and strict patient selection aimed to achieve the best primary stability. These various protocols need to be further documented in order to assess their predictability.

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About 20 years ago, Brånemark et al. (1977) published the first long-term follow-up study on oral implants, providing the scientific foundation of modern dental implantology. The predictability of implant integration according to Brånemark and collaborators (Brånemark et al. 1977; Adell et al. 1981; Albrektsson et al. 1981; Brånemark 1983) was obtained by adherence to a strict surgical and prosthodontic protocol. One of the most emphasized requirements was a stress-free healing period of 3–6 months (Brånemark et al. 1977; Adell et al. 1981; Albrektsson et al. 1981; Brånemark 1983; Brånemark et al. 1985; Albrektsson et al. 1986), making implant treatment lengthy. Presently however, early and immediate loading protocols are reported by an enhancing number of clinical (Ledermann 1984; Schnitman et al. 1990; Henry & Rosenberg 1994; Salama et al. 1995; Spiekerman et al. 1995; Balshi & Wolfinger 1997; Chiapasco et al. 1997; Schnitman et al. 1997; Tarnow et al. 1997) and experimental (De-

porter et al. 1986; Hashimoto et al. 1988; Lum et al. 1991; Akagawa et al. 1993; Piattelli et al. 1993a; Sagara et al. 1993; Piattelli et al. 1997a; Corso et al. 1999) publications. The purpose of this paper is therefore to clarify why Brånemark and collaborators (Brånemark et al. 1977; Adell et al. 1981; Brånemark 1983; Albrektsson 1983; Zarb & Jansson 1985; Albrektsson et al. 1986) required for osseointegration a delayed loading period of at least 3–6 months. In addition, it is aimed to discuss what has been gained during the last 20 years in order now to look at certain defined premature loading protocols involving delayed loading periods less than 3 months, as a potential predictable modality in implant therapy.

The Brånemark protocol

Before introduction of the Brånemark protocol, dental implants were commonly loaded at placement because immediate bone stimulation was considered to avoid crestal bone loss (Linkow & Cherchève 1970). Fibrous tissue interposition was considered the optimal response to implants as it was mimicking the natural periodontal ligament (Linkow & Cherchève 1970). In contrast to all other experimental studies of that time, Brånemark et al. (1969) showed that direct bone apposition at the implant surface was possible and lasting under loading at the condition that implants were left to heal in a submerged way. Following their 10-year clinical experience (Brånemark et al. 1977), recommendations ensuring durable osseointegration of dental implants were set. The most important were: 1) Use of a biocompatible material, i.e. titanium (Brånemark et al. 1977; Albrektsson et al. 1981); 2) Use of a 2-stage procedure (Brånemark et al. 1977; Adell et al. 1981; Albrektsson et al. 1986); 3) Use of a stress-free healing period of 3–6 months before loading (Brånemark et al. 1977; Albrektsson et al. 1981; Brånemark 1983; Zarb & Jansson 1985; Albrektsson et al. 1986); 4) Use of an atraumatic surgery involving low-speed drilling (Brånemark et al. 1977; Adell et al. 1981); 5) Use a mucobuccal incision and avoid a crestal one (Brånemark et al. 1977; Adell et al. 1981, 1985); 6) Use of sterile conditions as "in a fully equipped operatory" (Adell et al. 1985); 7) Use of titanium ancillary (Adell et al. 1985); 8) Avoid X-radiographs before the end of the healing period (Brånemark et al. 1977; Albrektsson et al. 1986) and 9) Use of acrylic occlusal contact surfaces (Adell et al. 1981; Skalak 1983; Skalak 1985).

Early loading was identified as a critical determinant for osseointegration by Brånemark et al. (1977). During the course of their clinical trial (Brånemark et al. 1977), various delayed loading periods were tried. In 1968, the mean healing time was 84 days, in 1970 it was as low as 45 days including some prosthesis loaded after 2–4 weeks. Having noted that "insufficient healing time was greatly increasing the risk of immediate or late implant mobility" (Brånemark et al. 1977), it was further enhanced, reaching 174 days in 1974 and then 89 days in 1975 (Table 1). Consequent to their 10-year clinical experience, they asserted that osseointegration requires a long healing period of at least 3 months in the mandible and at least 5–6 months in the maxilla (Brånemark et al. 1977; Adell et al. 1981; Zarb & Jansson 1985; Albrektsson et al. 1986). The rationale for such a long delayed loading period was that premature loading may lead to fibrous tissue encapsulation instead of direct bone apposition (Albrektsson 1981; Albrektsson et al. 1986). The second argument was that the necrotic bone at the implant bed border is not capable of load-bearing and must be first replaced by new bone (Brånemark et al. 1977; Brånemark 1983; Albrektsson et al. 1986). Two other reasons could be found in the literature, "rapid remodeling of the dead bone layer compromises the strength of the osseous tissue supporting the bone–implant interface" (Roberts et al. 1984), and "integrity of the periosteal margin may be threatened by undermining remodeling of adjacent bone during the late healing period" (Roberts et al. 1989).

Premature loading protocols

Nevertheless, loading protocols implying healing under loading were introduced. Ledermann (1979) used immediately loaded TPS (titanium plasma-sprayed) screw implants (Straumann Institute, Waldenburg, Switzerland) to stabilize overdentures in the mandible. The protocol called for 3–4 rough self-tapped implants inserted in the anterior part of the mandible, long enough to get bicortical anchorage. Implants were splinted and loaded the same day. Ledermann (1984) reported on a 1–81 months follow-up based on 476 implants placed in 138 patients. The survival rate (for definition of success rate vs survival rate, c.f. remark in Table 2) was 91.2% as 42 implants were explanted. Most failures occurred during the first year (34/42, 81%). Failures were accounted for lack of primary stability, lack of splinting, lack of at least 11 mm of available bone, buccal or lingual perforation, too early insertion in an extraction socket and insufficient hygiene.

Following the Ledermann protocol, Schroeder et al. (1983) inserted 53 ITI-type F cylinders (Straumann Institute, Waldenburg, Switzerland), a hollow-cylinder implant with a titanium plasma-sprayed surface, in 14 patients to support overdentures in the mandible. In the 5–48 month follow-up (mean 17.5 months), 1 implant failed due to perforation of the

Table 1. The mean healing periods used during the Brånemark (Brånemark et al. 1977) clinical study (1968–1975) are displayed according to the study step and the protocol. Long healing periods were initiated at starting the routine period. They were drawn from non-optimized anterior conditions involving "continuous adjustments and modifications of the therapeutic procedures" (Brånemark et al. 1977). Under less demanding conditions, shorter healing periods might have been successful. Initiation period was September 1965–March 1968, development period was April 1968–June 1971 and routine period was July 1971–June 1975

Year	Mean healing period (days)	Study stage	Protocol status
1965	no loading	Initiation period	Implant design modifications + Surgical protocol modifications + Demanding prosthetic biomechanics + Negative selection of patients
1966	no loading		
1967	n.a		
1968	84	Development period	
1969	68		
1970	45		
1971	77		
Assessment for longer healing periods, in the 3–6 months range			
1972	116	Routine period	Definitive implant design + Refined surgical protocol + Prosthetic amelioration + Negative selection of patients
1973	124		
1974	175		
1975	89		

lower corticalis, corresponding to a success rate of 98.1%. In 3 more patients, 4 ITI-type F cylinders inserted in the anterior part of the mandible supported immediately loaded bridges; after 19–22 months of follow-up no failure was recorded. The authors reported also on 3 maxillae restored with an overdenture retained on 2 implants (17-month follow-up) and 2 bridges supported by 2 and 4 implants, with respectively 17 and 7 months of follow-up. No failure was reported.

Babbush et al. (1986) replicated the Ledermann protocol on implant-retained overdentures (Ledermann 1979). Four TPS implants were placed in the anterior part of the mandible, they were splinted within 2–3 days by the mean of a Dolder bar and loaded. The survey was based on 129 patients and 514 implants with an up-to 5.5 years follow-up. During this period, 20 implants failed corresponding to a success rate of 96.1%. All failures occurred during the first year, whereas most of them (16/20, 80%) happened during the first 6 months. The 3-year follow-up concerned 122 implants inserted in 31 patients and success rate was unchanged. The opposing dentition, either natural or artificial, was not found to have any effect on implant survival. Failures were related to delayed splinting and perforation of the inferior border with secondary infection.

In edentulous mandibles rehabilitated by implant-retained overdentures, Dietrich et al. (1993) compared the outcome of 421 TPS screws with a mean follow-up of 57.1 months and 1137 IMZ (Friatec, Mannheim, Germany) cylinders with a mean follow-up of 37.6 months. The 2 implant systems differed in design and in surgical protocol. The IMZ implants were placed according to the 2-stage technique and the TPS implants were immediately splinted and loaded. After 6 months, the success rate of the TPS implants was 92.5% while it was 99.3% for the IMZ implants. At 5 years of follow-up, 86.3% of the TPS implants were still in function, compared to 94.6% for the IMZ implants. The authors found that healing mode was a statistically significant parameter for implant prognosis and concluded that immediate loading was leading to a higher failure rate.

In an up to 10 years follow-up, Spiekerman et al. (1995) reported on overdentures retained by mainly 3 TPS implants splinted in an angled bar and immediately loaded. Eleven patients received 36 implants, 1 implant failed during the first year. The 5-year follow-up led to a survival rate of 97.3% (1/36 failure).

Chapiasco et al. (1997) published a retrospective multicenter study on 226 edentulous patients restored with immediately-loaded implant retained overdentures. Four implants inserted in the anterior part of the mandible were rigidly connected by an U-shaped curved bar 1 day after placement. The 904 placed implants were distributed among 4 different implant systems: 380 TPS implants (Straumann Institute, Waldenburg, Switzerland) with a mean follow-up of 8.6 years (6–13 years), 152 ITI implants (Straumann Institute, Waldenburg, Switzerland) with a mean follow-up of 7.7 years (5–9 years), 208 Ha-Ti implants (Matthys Dental, Bettlach, Switzerland) with a mean follow-up of 3.2 years (2–6 years) and 164 NLS implants (Friatec, Mannheim, Ger-

Table 2. Clinical studies and case reports of prematurely loaded implants (<3 months) are displayed. They are divided into early and immediate loading protocols. Immediate loading protocols are separated according to rehabilitation type, overdenture and fixed bridge, that are then split into restoration at the mandible and maxilla

Loading time	Splinting time	Situation	Prosthetic rehabilitation	Immed. loaded implant no.	Implant type	Follow-up	No. of patients/ No. of implants	Success rate (a or b)	Reference
Early loading of fixed bridges									
7–9 weeks	7–9 weeks	Mand. anterior	Bilat. bridge	4	Brånemark	2 years	5p/20i	100% (b)	Henry & Rosenberg 1994
Immediate loading of overdentures									
<1 day	<1 day	Mand. anterior	Overdenture	3–4	TPS	1–81 months	138p/476i	91.2% (a)	Ledermann 1984
<1 day	<1 day	Mand. anterior	Overdenture	3–4	TPS	6 months	106p/421i	92.5% (a)	Dietrich et al. 1993
<1 day	<1 day	Mand. anterior	Overdenture	3	TPS	up to 10 years	11p/35i	97.3% (a)	Spiekermann et al. 1995
1 day	1 day	Mand. anterior	Overdenture	4	ITI-Type F	17 months (5–48)	14p/53i	98.1% (a)	Schroeder et al. 1983
1 day	1 day	Mand. anterior	Overdenture	4	TPS	8.6 years (6–13)	84p/336i	96.7% (b)	Chiapasco et al. 1997
1 day	1 day	Mand. anterior	Overdenture	4	ITI	7.7 years (5–9)	31p/124i	96.8% (b)	Chiapasco et al. 1997
1 day	1 day	Mand. anterior	Overdenture	4	NLS	4.8 years (4–6)	34p/136i	96.3% (b)	Chiapasco et al. 1997
1 day	1 day	Mand. anterior	Overdenture	4	Ha-Ti	3.2 years (2–6)	45p/180i	97.2% (b)	Chiapasco et al. 1997
2–3 days	2–3 days	Mand. anterior	Overdenture	4	TPS	up to 5.5 years	129p/514i	96.1% (a)	Babbush et al. 1986
1 day	1 day	Max. anterior	Overdenture	2	ITI-Type F	17 months	3p/6i	100% (a)	Schroeder et al. 1983
Immediate loading of fixed bridges									
Immediate	Immediate	Mand.	Bilat. bridge	2*	Brånemark	2 years	1p/2i	100% (a)	Salama et al. 1995
Immediate	Immediate	Mand.	Fixed rehab.**	1–6***	Brånemark	up to 10 years	10p/28i	85.7% (b)	Schnitman et al. 1997
Immediate	Immediate	Mand.	Bilat. bridge	4–5*	Brånemark	3–5 years	4p/20i	90% (a)	Tarnow et al. 1997
Immediate	Immediate	Mand.	Bilat. bridge	6*	ITI	4 years	1p/6i	100% (a)	Tarnow et al. 1997
Immediate	Immediate	Mand.	Bilat. bridge	10	Astra	2 years	1p/9i	100% (a)	Tarnow et al. 1997
Immediate	Immediate	Mand.	Bilat. bridge	4*	Brånemark	1–1.5 years	10p/40i	80% (b)	Balshi et al. 1997
Immediate	Immediate	Max.	Bilat. bridge	3*	3i cylinders	2 years	1p/3i	100% (a)	Salama et al. 1995
Immediate	Immediate	Max.	Bilat. bridge	2*	Brånemark	2 years	1p/2i	100% (a)	Salama et al. 1995
Immediate	Immediate	Max.	Bilat. bridge	6–8*	Brånemark	2–4 years	2p/14i	100% (a)	Tarnow et al. 1997
Immediate	Immediate	Max.	Bilat. bridge	10	Astra	1 year	1p/10i	100% (a)	Tarnow et al. 1997
Immediate	Immediate	Max.	Bilat. bridge	10	3i	1 year	1p/10i	100% (a)	Tarnow et al. 1997

*=Number of loaded implants between surgery-1 and surgery-2, the final prosthesis relies on "primary" and "secondary" implants; **=1 patient had a unilateral fixed bridge; ***=1 patient had 1 implant immediately loaded with 2 natural teeth. (a) When not explicit in reports, success rate is determined according to clinical immobility, i.e. survival rates (Albrektsson & Sennerby 1991). (b) When provided by the authors, success rate is based on clinical mobility and bone loss <0.2 mm annually (Albrektsson & Sennerby 1991).

many) with a mean follow-up of 4.8 years (4–6 years). Bicortical engagement was achieved whenever possible and implants ≥10 mm were used. The prosthetic fit was carefully checked. Success criteria included an annual bone loss <0.2 mm. They reported a success rate of 96.9%; most failures happened during the first year (10/15, 66.66%), 3 in the second year of service and 2 others after 5 years. No significant relationship was found between failure and implant system (c.f. Table 2).

In 10 patients that refused to wear removable appliances, Schnitman et al. (1990, 1997) inserted 63 Brånemark implants (Nobel Biocare, Göteborg, Sweden) 7 to 15 mm long; 28 implants were loaded at placement to support provisional fixed prostheses. The latter implants were arranged in a broad-based tripod with restorations relying either on implants (6 patients) or on implants and remaining teeth (3 patients). This permitted the other submerged implants to heal in the traditional way. The immediately loaded implants were supposed to fail and were considered as "disposable implants" (Schnitman et al. 1990). Strikingly, at stage surgery-2 most of them were not mobile, therefore they were incorporated in the final bilateral bridges. Encouraged by these results, patient #6 had all his 6 implants immediately loaded. After up to 10 years of follow-up, 4 out of the 28 immediately loaded implants failed, 2 were 7 mm long implants, 1 was 10 mm and 1 was 15 mm, corresponding to a success rate of 85.7%. None of the 35 submerged implants failed. Most failures occurred during the first 6 months (3/4, 75%), 1 implant failed after 21 months. The authors stated that "statistical analysis of submerged versus immediately loaded implants demonstrated failures rates to be significantly higher" (Schnitman et al. 1997). They suggested that bone quality more than implant length was a survival factor since 3 out of 4 failures happened distal to the mental foramina where bone density decreases.

Following the provisional fixed restoration principle described by Schnitman et al. (1990), Salama et al. (1995) treated 2 patients with "secondary" (immediately loaded) and "primary" implants (submerged) (Salama et al. 1995). Patient # 1 received in the maxilla 3 "primary" and 3 "secondary" cylindrical implants (3i, Palm Beach Gardens, Florida). In patient #2, Brånemark implants were placed; in the mandible, they were 2 "primary" and 2 "secondary" implants and in the maxilla, 4 "primary" and 2 "secondary" implants. By the end of the healing period, the "secondary" implants were not mobile, they were incorporated in the final bilateral bridge. At the 3-year follow-up no implant failed.

In 10 patients, Tarnow et al. (1997) evaluated implant screws immediately loaded with a fixed provisional restoration. Implants were belonging to various implant systems (c.f. Table 2). Six edentulous mandibles and 4 edentulous maxillae were treated with at least 10 mm long implants and followed during 1 to 5 years. A minimum of 10 implants were placed in each patient. In the first 6 patients, at least 5 screws were allowed to heal without load as a security. In patients # 7 and # 8, the number of submerged implants was decreased; in the last 2 patients all 10 implants were immediately loaded because it has been observed that implants integrated in the previous patients. Sixty-seven out of 69 (97.1%) immediately loaded implants integrated as well as 37 out of 38 (97.4%) submerged implants. The authors concluded that immediate loading of bilaterally splinted implants can be a viable treatment modality.

Similarly, Balshi & Wolfinger (1997) published a 12–18 month survey on immediately loaded Brånemark implants in the mandible. In 10 patients, 130 implants were inserted with a minimum of 10 implants per patient. The transitional fixed implant-supported prosthesis were relying on 4 implants. Implant length was at least 7 mm in the posterior region, bone quality varied from type II with thick cortical bone to type IV with thin cortical plates and loose trabecular bone (Lekholm & Zarb 1985). By the end of the survey, 32 out of 40 immediately loaded implants (80%) and 86 out of 90 submerged implants (95.6%) were clinically stable. They stated that this study suggests that premature loading of dental implants will adversely affect the survival rate for integration. A relationship between implant failure and bone quantity, implant site or opposing occlusion was not found. However, they suggested that bone quality was an important factor since no failure occurred in bone type II.

Early loading of implants inserted in the anterior part of the mandible was reported by Henry & Rosenberg (1994). In 5 edentulous patients, 6 Brånemark implants were placed with bicortical anchorage; 4 of them were left non-submerged and were loaded with a bilateral bridge after 7–9 weeks of healing. The 2 remaining implants were kept as sleepers to activate in case of failure. Implant length varied from 7 to 15 mm and bone quality was type II in 4 patients and type IV in 1 patient. At the 2-year follow-up, no implant was lost. They suggested that after 7–9 weeks, the "time frame of bone implant interface development appears to have sufficient load-bearing capacity to support a bridge with reduced cantilever extensions" (Henry & Rosenberg 1994).

Discussion

Although the aforementioned clinical papers dealing with early and immediately loaded implants re-

ported on clinical implant stability, this alone is not enough to assert that osseointegration occurred. It can be that a thin fibrous layer has developed at the bone-implant and because its reduced thickness, clinical immobility is still assessed at the short- or mid-term. This thin layer may become thicker with time and jeopardize implant success (Brånemark 1983). Therefore, experimental work is necessary to support the hypothesis that osseointegration can be achieved when healing under loading is allowed. This issue has been addressed by several authors (Deporter et al. 1986; Hashimoto et al. 1988; Lum et al. 1991; Akagawa et al. 1993; Piattelli et al. 1993a; Sagara et al. 1993; Piattelli et al. 1997a; Corso et al. 1999) and one can find a literature review providing such evidence when implants are splinted into a bridge framework (Szmukler-Moncler et al. 1998). In addition, retrieved human samples of immediately loaded implants (Linkow 1992; Piattelli et al. 1993a, 1997b) substantiate the hypothesis that osseointegration can be obtained. These clinical and experimental reports make necessary to understand why Brånemark and co-workers (Brånemark et al. 1977; Adell et al. 1981, 1985; Albrektsson et al. 1981, 1986) came to the conclusion that a long-delayed loading period was a prerequisite to implant integration. The following attempts to clarify it.

Brånemark et al. (1977) reported that their implant rehabilitation trial was divided into 3 different periods: the initial period between September 1965 and March 1968, the development period between April 1968 and June 1971 and the routine period between July 1971 and June 1975. Before starting the routine period the protocol underwent various modifications (Brånemark et al. 1977) as shown on Table 1. The mean healing time was less than to the 3–6 month period that was further maintained during the routine part of the study (c.f. Table 1). Conclusion that "a minimum healing period of 3 months is required, otherwise the risk of immediate or late implant mobility greatly increases" (Brånemark et al. 1977) was drawn before starting the routine period, from particularly demanding clinical conditions.

In effect, patient selection was "a negative selection with patients exhibiting an extremely resorbed jaw bone of often low mechanical strength" (Brånemark et al. 1977), where 10% had moderate bone resorption, 80% had advanced resorption and 10% had extreme resorption (Brånemark et al. 1977). These patients had "often a fairly thin cortex with a central marrow space, containing few osseous trabeculae providing less favorable mechanic retention of the implant" (Brånemark et al. 1977). It is presently admitted that bone quality is a determinant parameter for implant prognosis. Higher failure rates were recorded for submerged implants inserted in recipient sites with thin cortical bone (Jaffin & Berman 1991; Saadoun & LeGall 1992; Jemt 1993; Hutton et al. 1995). Therefore, the patient population that led to the requirement of a minimum of 3–6 months of delayed loading did not represent a patient pool with good bone conditions, e.g. type I or II where a thick cortical bone is present (Lekholm & Zarb 1985).

Second, implant design differed from present Brånemark implant in dimension and design since "standard dimensions and proportions were established from the routine period and onwards" (Brånemark et al. 1977). Before the routine period, up to 22 implant designs have been tried and abandoned (Brånemark et al. 1977). It comes out that the various implant designs that led to the requirement of a minimum of 3–6 months of delayed loading were not optimized.

Third, the surgical protocol was not optimal since "continuous adjustments and modifications of therapeutic procedures" occurred (Brånemark et al. 1977). Up to the routine period, "fairly extensive muco-periosteal flaps" were raised (Brånemark et al. 1977). "This approach especially deprived the cortical bone jaw from part of its periosteal vascular supply" (Brånemark et al. 1977) and delayed bone healing. While "in the routine period reduced bone exposure led to less post-operative complications and enhanced bone healing" (Brånemark et al. 1977). Moreover, "when short fixtures were placed rather superficially the covering bone was often fairly thin especially marginally. In the routine procedure, longer fixtures were used which were also inserted deeper within the jaw bone. This means that there were considerably more bone tissue surrounding the implant at installation" (Brånemark et al. 1977). Today, it has been documented that length is a critical parameter for implant integration (Quirynen et al. 1992; Bahat 1993; Henry et al. 1993; Higuchi et al. 1995). In addition, tapping was part of the surgical protocol (Brånemark et al. 1977). Tapping affects the holding power of screw implants; noteworthy, Schnitman et al. (1990, 1997) and Salama et al. (1995) in their immediate loading protocols reduced or avoided tapping, in order to provide the best primary stability.

Fourth, because most patients presented advanced or severely resorbed jaws, the prosthetic rehabilitations presented "unfavorable load conditions due to long abutments levers" (Brånemark et al. 1977) and angled loading (Brånemark et al. 1977). In addition, "in the development stage, the design of bridges could not be given priority because of the limited resources of the group. Having

established that the method of anchoring via osseointegration had a good prognosis, the bridge construction was refined" (Brånemark et al. 1977). Therefore, the prosthetic biomechanics that led to the requirement of a minimum of 3–6 months of delayed loading was very demanding.

Thus, the principle of a 3–6 months delayed-loading period advocated by Brånemark et al. (1977) was drawn from specially demanding clinical situations involving simultaneously: 1) patient selection with poor quality and quantity bone, 2) non-optimized implant design, 3) short implants, 4) non-optimized surgical placement, 5) non-optimized surgical technique and 6) biomechanically demanding prosthesis. It was then set as a general requirement (Adell et al. 1981; Brånemark 1983; Albrektsson et al. 1986). It is legitimate to question if this extrapolation applies to more standard conditions, involving recipient sites with better bone quality and quantity, refined surgical and prosthetic protocols and different implant design.

Nevertheless, 15–20 years ago, a strict protocol was imperative to warrant the highest predictability to implant therapy. It was aimed to struggle against disrepute and to convince the professional community that implants might be considered as *lege artis* in dentistry (Brånemark et al. 1977). To achieve this goal, the stress-free healing period had to be considered as an absolute prerequisite to achieve osseointegration (Adell et al. 1981; Albrektsson et al. 1981; Albrektsson et al. 1986) because it was a no-risk situation. Consequently, however, it was commonly understood that premature loading was jeopardizing the process of osseointegration (Schnitman et al. 1990; Henry & Rosenberg 1994; Salama et al. 1995; Balshi & Wolfinger 1997; Chiapasco et al. 1997; Tarnow et al. 1997) whereas it was originally defined as "an increasing risk" (Brånemark et al. 1977). It should be stressed that in that clinical trial, no number was given stipulating a clear correlation between healing time and implant failure. It was impossible to provide "detailed statistical analysis of separate parameters – like the healing period – as a consequence of the heterogeneous composition of the clinical material in this development project and the continuous adjustments and modifications of therapeutic procedures" (Brånemark et al. 1977).

Today however, high levels of predictability in implant therapy have been demonstrated. This has encouraged re-evaluation of several aspects of the traditional Brånemark implant protocol (Cibirka et al. 1992; Quirynen et al. 1992; Weber et al. 1992; Scharf & Tarnow 1993; Basquill et al. 1994; Hürzeler et al. 1995). The first re-evaluated requirement was the need for a 2-stage procedure. In the 70s, Schroeder et al. (1976, 1978, 1981) showed that the submerged technique was not a prerequisite to the achievement of osseointegration. This was further documented by various experimental (Godfredsen et al. 1991; Piattelli et al. 1993a; Weber et al. 1996) and clinical reports (Buser al. 1990, Weber et al. 1992; Mericske-Stern & Zarb 1993; Bernard et al. 1995b). In several animal studies, osseointegration has been reported even when implants designed for the submerged procedure were placed according to the one-stage technique (Abrahamsson et al. 1996; Ericsson et al. 1996; Levy et al. 1996). Clinical trials using the above feature observed no difference between the 2 approaches, at least at the short-term (Ericsson et al. 1994; Henry & Rosenberg 1994; Bernard et al. 1995a; Barber et al. 1996; Becker et al. 1997) or the mid-term (Ericsson et al. 1997). Henry & Rosenberg (1994) suggested that "considerable flexibility probably exists in the procedure" originally advocated by Brånemark and collaborators (Brånemark et al. 1977; Adell et al. 1981). Becker et al. (1997) concluded that "one-step Brånemark implants may be considered a viable alternative to two-step implants". Noteworthy, implants inserted according to the 1-stage technique are left transgingival during the healing period; thus they are submitted to a higher amount of load when compared to the 2-stage technique. Under this more demanding mechanical environment, osseointegration is still achieved.

In the past, it has been asserted that "too-early loading of an implant leads to interfacial formation of fibrous tissue instead of bone" (Albrektsson et al. 1986). Presently, it appears that premature loading *per se* does not lead to fibrous tissue encapsulation. Rather, it is due to an excessive amount of micro-motion at the bone–implant interface, during the healing phase (Pilliar 1991; Brunski 1992; Szmukler-Moncler et al. 1998). The existence of 2 distinct types of motion at the interface has been recognized by Cameron et al. (1973) when studying bone ingrowth into porous Vitallium staples in a dog model. On one hand, micromotion was not found to prevent bone ingrowth (Cameron et al. 1972); on the other hand, motion of approximately 200 μm resulted in fibrous tissue integration instead of bone ingrowth (Cameron et al. 1973). Tolerance to micromotion was also observed by Maniatopoulos et al. (1986). They inserted endodontic implants with 2 distinct designs, screws and porous cylinders, in bone through the endodontic canal of the incisors and through the interradicular bridge of the molars. Mastication following implantation was immediately allowed and led to implant micromotion via the periodontal ligament, estimated to be in the 30 μm range (Pilliar 1991). The authors found that after 3 months, the porous cylinders osseointe-

grated while the screws were encapsulated by a fibrous membrane. Under the same amount of micromotion, only the porous endodontic implants osseointegrated (Maniatopoulos et al. 1986). This suggests that micromotion does not systematically lead to fibrous tissue interposition, that tolerance to micromotion is design and/or surface dependent. Pilliar et al. (1995) in a controlled micromotion model in the dog mandible showed that micromotion of up to 50 μm was tolerated for porous conical cylinders. The threshold for tolerated micromotion was found to be higher than 30 μm as previously thought (Pilliar 1991). Søballe et al. (1992, 1993), in a different controlled micromotion model involving the dog femur, showed that 150 μm of micromotion were tolerated by calcium phosphate (CaP) coated titanium alloy (TiAlV) implants. Under the same loading conditions, the titanium alloy plasma-spayed implants (without the CaP layer) were encapsulated in fibrous tissue. When submitted to 500 μm of micromotion, the CaP-coated and the non-coated TiAlV implants failed to osseointegrate (Søballe et al. 1992). This indicates that the threshold level of tolerated micromotion lies somewhere, for roughened bioinert surfaces, between 50 and 150 μm. In addition and as reported by others, the presence of a CaP layer enhances tolerance to micromotion (Geesink et al. 1987; Thomas et al. 1989; Søballe et al. 1993; Lum et al. 1991; Oonishi et al. 1994; Szmukler-Moncler et al. 1996).

Hence, conjunction of the 4 following reasons may provide cause to re-evaluate the mandatory aspect of a long delayed loading period. They are: 1) take into consideration the specifically demanding conditions met during the original Brånemark follow-up (Brånemark et al. 1977); 2) loading *per se* does not impede the healing process to occur; 3) prematurely loaded implants are capable of integration as demonstrated in several experimental studies (Deporter et al. 1986; Hashimoto et al. 1986; Akagawa et al. 1993; Piattelli et al. 1993a; Sagara et al. 1993; Piattelli et al. 1997a; Corso et al. 1999); 4) prematurely loaded implants are capable of clinical integration as observed by various authors (Ledermann 1984; Schnitman et al. 1990, 1997; Salama et al. 1995; Balshi & Wolfinger 1997; Chiapasco et al. 1997; Tarnow et al. 1997).

However, in order to assess how early after placement a loading protocol should be considered as premature, healing periods need first to be clinically ascertained because it must be realized that presently recommended delayed loading periods have been "empirically estimated" (Brånemark et al. 1977). Hence, for patients that cannot wait the recommended 3–6 month delayed loading period (Schnitman et al. 1990; Henry & Rosenberg 1994; Salama et al. 1995; Balshi & Wolfinger 1997; Tarnow et al. 1997), predictable loading protocols involving shorter healing periods need to be developed. Two different approaches are relevant, one is to optimize the healing period before a safe functional loading can be exerted on free-standing implants. This should be achieved by reducing stepwise the delayed loading periods, below the traditional 3–6 months. The second option is to identify, upon immediate loading, an effective way to reduce micro-motion beneath the critical threshold of deleterious micro-motion.

Optimization of the healing period for free-standing implants

In the light of the demanding clinical conditions of the Brånemark follow-up (Brånemark et al. 1977), it is speculated that a high level of predictability might be expected for healing periods inferior to 3 months in the mandible, e.g. 10 to 6 weeks. However, they still need to be documented by clinical trials involving cautious stepwise reductions of the delayed loading periods. In 5 patients, Henry & Rosenberg (1994), loaded 4 implants with a bilateral bridge after 7–9 weeks of healing. It cannot be concluded that these implants were integrated and would have been able to support free-standing crowns. Those implants were splinted when submitted to functional load, and splinting could have reduced the amount of tolerated micromotion below the critical threshold of deleterious micromotion.

When setting-up clinical trials with healing periods inferior to 3 months, various factors should be taken into account. First, the healing period might be modulated according to the recipient site quality, as suggested in the past for standard protocols (Brånemark et al. 1977; Albrektsson et al. 1986). Shorter healing periods should be rather applied to bone type I and II since under the traditional protocol, implant prognosis is significantly affected by bone quality (Jaffin & Berman 1991; Saadoun & LeGall 1992; Jemt 1993). Second, implant surface may also be a relevant parameter. For example, it is suggested that implants with a rough surface obtained by titanium plasma-spraying might be loaded earlier. This is because titanium plasma-sprayed surfaces when compared to smooth surfaces, have shown to foster bone apposition (Kirsch & Donath 1984), to achieve a higher amount of bone apposition (Buser et al. 1991) and stronger fixation during the healing phase as measured by the torque method (Claes et al. 1976; Wilke et al. 1990). Similarly, it can be speculated on shorter delayed loading periods for CaP-coated screws when compared to similar machined implants, since higher levels of

bone apposition were found during the healing phase by several authors (Gottlander & Albrektsson 1991; Gottfredsen et al. 1995) and significantly higher removal torque have been measured (Carr et al. 1995; Godfredsen et al. 1995). Nevertheless, extrapolation of this hypothesis to CaP coated screws in general is not relevant because significant performance variability has been found among CaP-coatings (Dalton & Cook 1995). This is due to the dramatic influence of plasma-sprayed parameters on the biologic outcome of CaP coatings.

Immediate loading protocols reducing micro-motion beneath the threshold of deleterious micro-motion

The second way to shorten the delayed loading period is to find an effective prosthetic option that maintains the amount of micro-motion beneath the threshold of deleterious micromotion during the healing phase. This has been tried for implant-retained overdentures and fixed rehabilitations (Fig. 1). In edentulous patients treated with overdentures, the splinting of 3–4 implants in the interforaminal area aimed to reduce the amount of micromotion was successful up to a certain extent (Table 2). The success rates reported by Babbush et al. (1986) and Chiapasco et al. (1997) are comparable to those reported in the literature for implant-retained overdentures with implants healed in the traditional way (Mericske-Stern & Zarb 1993; Hutton et al. 1995). However, Dietrich et al. (1993) found this immediate loading protocol to be less predictable than the delayed one. This shows that loading during the healing phase is indeed increasing the failure risk (Brånemark et al. 1977) but still osseointegration can be obtained. Most failures occurred during the first year of service (Ledermann 1984; Babbush et al. 1986; Dietrich et al. 1993; Chiapasco et al. 1997) which is in accordance with the observation of Brånemark et al. (1977) that when clinical immobility is maintained during the first year of function, the risk for a later mobility is decreased. To be predictable, this modality warrants a careful patient selection, where bicortical anchorage in adequate bone quality and implant length are of paramount importance (Chiapasco et al. 1997).

For implant-retained fixed restorations, 2 alternatives have been described (Fig. 1). The first one developed by Schnitman et al. (1990) involves insertion in the anterior and posterior regions of "primary and secondary implants" (Salama et al. 1995). The latters sustain a provisional prosthesis in a broad-based tripod configuration and permit the "primary" implants to heal in the traditional way. At the end of the 3-month healing period, the clinically immobile "secondary" implants and the "primary" implants are incorporated in a definitive restoration (Schnitman et al. 1990; Salama et al. 1995; Balshi & Wolfinger 1997; Tarnow et al. 1997). The second way involves a higher number of implants, 6 to 10 implants, all immediately loaded in the provisional restoration (Schnitman et al. 1990; Tarnow et al. 1997). As seen in Table 2, published reports are scarce and should be still considered anecdotal. Patently, Schnitman et al. (1997)

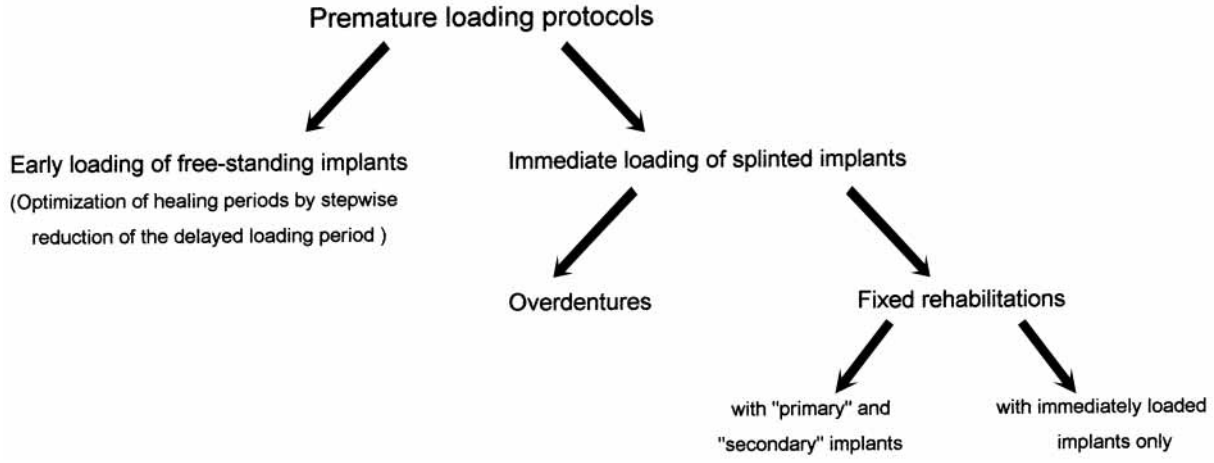

Fig. 1. Premature loading protocols that had to be investigated for predictability are shown. These protocols are divided according to 2 options. One is to reduce stepwise the delayed loading period for free standing implants, beneath the presently recommended 3–6 months of healing. The second option is an immediate loading protocol with implant splinting, in order to reduce micromotion within the tolerated amount of micromotion. It applies to overdentures or to bilaterally fixed bridges. The fixed rehabilitation protocol may follow 2 ways. One involves "secondary" (immediately-loaded) and "primary" implants (non-loaded) (Salama et al. 1995). The "secondary" implants support a fixed provisional restoration up to the end of the healing period, then "primary" implants and non-mobile "secondary" implants are incorporated into the definitive fixed rehabilitation. The second way involves only immediately loaded implants, higher in number, without submerged implants in reserve.

and Balshi & Wolfinger (1997) found a prognosis difference between the immediately loaded and the delayed loaded implants. Tarnow et al. (1997) on the other hand did not experience such a disparity. This indicates that these immediate loading protocols increase the failure risk but still can lead to osseointegration. From these few studies, it can be learned that bone quality plays a critical role because no failure occurred in bone type II (Schnitman et al. 1997; Balshi & Wolfinger 1997). It is speculated that in addition to bone quality, a number of 6–10 "primary implants" of at least 10 mm in length should improve the prognosis of this treatment modality as suggested by Tarnow et al. (1997). Application of immediately loaded implants in the maxilla has been dissuaded by Schnitman et al. (1997) and Balshi & Wolfinger (1997); however, anecdotal cases have been successful (Salama et al. 1995; Tarnow et al. 1997). In conclusion, it appears that the various modalities of immediately loaded implant-retained prosthesis (Fig. 1) require a careful and strict patient selection aimed to achieve the best implant primary stability. Albeit non-well documented, they open intriguing treatment-planning possibilities (Salama et al. 1995; Schnitman et al. 1997).

Résumé

En implantologie buccale, une période de guérison de 3–6 mois sans stress direct sur l'implant est recommandée pour obtenir une bonne apposition osseuse sans interposition de tissu cicatriciel fibreux. Ce protocole a été introduit par Brånemark et al. en 1977. Le but de cette analyse est de revoir les raisons qui ont amené Brånemark et ses collaborateurs à exiger des périodes aussi longues. La nécessité d'avoir ces périodes de plusieurs mois avant de pouvoir mettre en charge les implants est a été tirée de leurs premières études et essais cliniques. Des conditions particulièrement difficiles étaient simultanément réunies-comprenant 1°) des patients avec une faible quantité et qualité osseuse, 2°) un dessin implantaire non-optimale, 3°) des implants courts, 4°) une technique chirurgicale non-optimale, 5°) un protocole chirurgical non-optimal, 6°) des prothèses biomécaniquement non-optimales. L'extrapolation de cette nécessité d'un temps de guérison prolongé pour ces conditions particulières aux situations plus standards avec des protocoles chirurgicaux affinés et une sélection de patients plus parfaite peut être revue. Bien que la charge prématurée ait été interprétée comme induisant une interposition tissulaire fibreuse, la charge immédiate par elle-même n'est pas responsable de l'encapsulation fibreuse. C'est l'excès de micromouvements durant la phase de guérison qui interfère avec la réparation osseuse. Un seuil de tolérance de ces micromouvements existe, se situant entre 50 et 150 µm. Les protocles de différé de mise en charge peuvent être diminués suivant deux types d'approche. La première serait de diminuer par étapes la période de différé de mise en charge pour des implants unitaires durant des périodes inférieures à celles de 3 à 6 mois présentement acceptées. La seconde serait d'identifier des protocoles de mise en charge immédiate susceptible de maintenir la quantité de micro-mouvements en deçà du seuil de tolérance. Les protocoles de mise en charge immédiate pour les prothèses amovibles et inamovibles sont passés en revue. Le protocole de mise en charge immédiate nécessite une sélection rigoureuse des patients visant à obtenir la meilleure stabilité primaire. Ces différents protocoles doivent être mieux documentés pour pouvoir prédire leur succès à plus long terme.

Zusammenfassung

In der oralen Implantologie wird im Moment eine drei- bis sexmonatige belastungsfreie Heilphase als Voraussetzung erachtet, um eine Knochenapposition ohne fibröse Zwischenschicht ans Implantat zu erhalten. Dieses Protokoll wurde 1977 von Brånemark und Mitarbeitern eingeführt. Das Ziel dieser Arbeit ist es nun, die Gründe zusammenzutragen, die Brånemark und seine Mitarbeiter dazuführten, so lange Einheilzeiten vor der funktionellen Belastung zu verlangen. Es wurde gezeigt, dass die Forderung nach langen Einheilzeiten vor der funktionellen Belastung aus der Anfangs- und Entwicklungsphase während den ersten klinischen Versuchen stammt. Gleichzeitig wurden wichtige Bedingungen für diese Forderung aufgestellt: 1) Patienten mit schlechter Knochenqualität und geringer Knochenquantität, 2) nichtoptimales Implantatdesign, 3) kurze Implantate, 4) nichtoptimale chirurgische Plazierung, 5) nichtoptimales chirurgisches Protokoll und 6) biomechanisch nichtoptimale Rekonstruktionen. Die Extrapolation der Forderung nach langen Einheilphasen auf Grund dieser speziellen Bedingungen für standartisiertere Situationen mit verfeinertem chirurgischem Protokoll und sorgfältiger Selektion des Patientengutes kann somit in Frage gestellt werden. Auch wenn die vorzeitige Belastung für die Induzierung einer Einlagerung von faserigem Gewebe zwischen Implantat und Knochen verantwortlich gemacht wird, ist die Sofortbelastung per se nicht verantwortlich für eine faserige Einkapselung. Es ist das Ausmass der Mikrobewegungen während der Heilphase, welches die Knochenreparation stört. Es existiert auch ein tolerierter Grenzwert der Mikrobewegungen, er liegt irgendwo zwischen 50 µm und 150 µm. Man schlug zwei Arten vor, die Zeit bis zur okklusalen Belastung zu verkürzen. Ein erster Vorschlag lautet, eine Belastungsperiode vor Ablauf der heute gültigen Heilphase von 3–6 Monaten mit schrittweiser Zunahme der Belastung von freistehenden Implantaten zu definieren. Der zweite Vorschlag geht dahin, eine Sofortbelastung zu erlangen, die das Ausmass der Mikrobewegungen unter der Schwelle der Schädlichkeit halten kann. Eine Übersicht von Arbeiten mit sofort belasteten implantatgetragenen Hybridprothesen und festsitzenden Brücken zeigt, dass die erfolgreiche Sofortbelastung eine sorgfältige und zurückhaltende Patientenauswahl erfordert, die darauf abzielt, die bestmögliche Primärstabilität zu erlangen. Zur Erlangung einer Voraussagbarkeit müssen jedoch die verschiedenen Protokolle weiterdokumentiert werden.

Resumen

En implantología oral, se acepta actualmente un periodo de cicatrización libre de estrés de 3 a 6 meses como un requisito previo para lograr una aposición ósea sin interposición de un tejido fibroso cicatricial. Este protocolo se introdujo por Brånemark y colaboradores en 1977. La intención del presente artículo es revisar las razones que llevaron a Brånemark y colaboradores a requerir periodos de carga tan largamente retrasados. Se ha demostrado que el requerimiento para periodos de carga largamente retrasados fue tomado desde los periodos iniciales y de desarrollo de su ensayo clínico original. Las condiciones demandantes se encontraron afectando simultáneamente, 1) pacientes con pobre calidad y cantidad ósea, 2) diseño no optimizado de implantes 3) implantes cortos 4) colocación quirúrgica no optimizada 5) protocolo quirúrgico no optimizado y 6) prótesis biomecánica no optimizada. La extrapolación de las necesidades para periodos de cicatrización largos a partir de estas condiciones particulares hacia situaciones más estándar inclu-

yendo protocolos quirúrgicos más refinados y una selección más cuidadosa de los pacientes puede ser cuestionada. Aunque la carga prematura ha sido interpretada como inductora de interposición de tejido fibroso, la carga inmediata per se no es responsable de encapsulación fibrosa. Es el exceso de micromoción durante de la fase de cicatrización que interfiere con la reparación ósea. Existe un umbral tolerado de micromoción, que está en algún sitio entre 50 μm y 150 μm. Se sugiere que los protocolos de carga puedan ser acortados a través de dos aproximaciones diferentes. La primera manera podría ser disminuyendo paulatinamente el periodo retrasado de carga para implantes libres por debajo de los 3 a 6 meses de cicatrización actualmente aceptados. La segunda manera podría ser identificando protocolos de carga inmediata que sean capaces de mantener la cantidad de micromoción por debajo del umbral de micromoción perjudicial. Los protocolos de carga inmediata para sobredentaduras implantoretenidas sobre puentes fijos están siendo revisadas. Se ha demostrado que los protocolos de carga prematura exitosos requiren una selección cuidadosa y estricta de los pacientes dirigidas a lograr la mejor estabilidad primaria. Estos diferentes protocolos necesitan ser más documentados en orden a lograr su predictabilidad.

要旨

口腔インプラント治療において、線維性瘢痕組織の介在なく骨の添加を達成するための必要条件として３－６ヶ月の非荷重の治癒期間が認められているが、このプロトコールは１９７７年に Branemark らが導入したものである。本稿では Branemark らが長期の荷重遷延期間を必要条件とした理由を検討する。長期荷重遷延期間は、彼らの当初の臨床試験の開始、開発時期に導き出された。１）骨質と量の乏しい患者、２）最適ではないインプラントのデザイン、３）短いインプラント、４）最適ではない埋入の術式、５）最適ではない外科的プロトコール、及び６）生体力学的に最適ではない補綴物という悪条件が併存する中で厳しい条件が設定された。これらの特別な条件下で設定された長い治癒期間という要件を、改良された外科的プロトコールと慎重な患者選択という、より標準化された状況にあてはめることの是非が問われる。早期荷重は線維組織の介在を起こすと解釈されているが、即時荷重そのものが線維形成を引き起こすのではない。認容しうる微小な動揺性の閾値が存在し、約５０μｍから１５０μｍの領域である。荷重プロトコールは異なる二つのアプローチを通して短縮することが示唆される。一つは単独植立しているインプラントの荷重遷延期間を現在認められている３－６ヶ月の治癒期間以下に段階的に減らしてゆく方法である。もう一つの方法は、微小動揺の量を有害な微小動揺の閾値以下におさえることができるような即時荷重のプロトコールを確立することである。インプラント支持によるオーバーデンチャーと固定式ブリッジの即時荷重のプロトコールを検討する。早期荷重プロトコールの成功には、最良の初期安定性を達成するために、慎重かつ厳密な患者選択が必要であることが示される。これらの様々なプロトコールは、その予知性を評価するために、さらに実証を重ねる必要がある。

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