

American Association of Oral and Maxillofacial Surgeons
94th Annual Meeting, Scientific Sessions and Exhibition

September 11-15, 2012 ♦ San Diego, CA

S117: Trigeminal Nerve Injuries

Dr. Michael Miloro

Wednesday, September 12, 2012

2:30pm - 4:30pm

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Trigeminal Nerve Disorders Diagnosis

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Professor

Department Head & Program Director

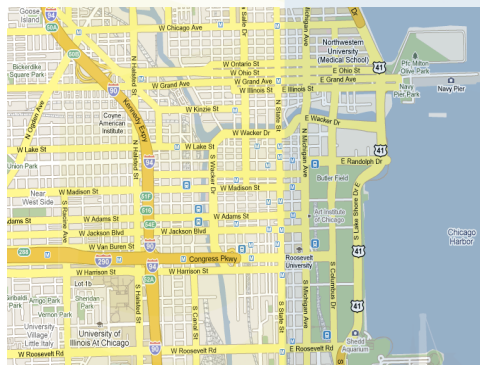
Oral and Maxillofacial Surgery

University of Illinois at Chicago

Chicago, Illinois

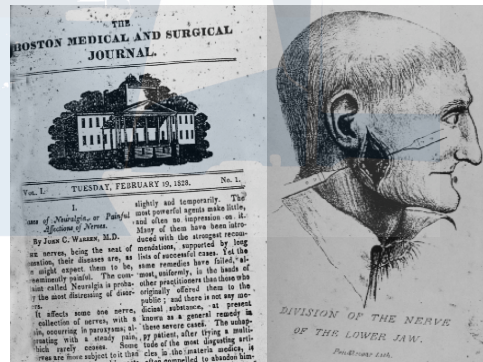


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Program Outline

- Etiology of nerve injuries
- Radiographic evaluation
- Nerve anatomy and physiology
- Clinical neurosensory testing
- Classification of nerve injuries
- Management

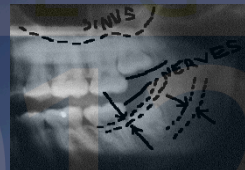


Top Malpractice Claims *J Calif Dental Assoc, 1996*

- 1. Extract wrong tooth
- 2. Dental implant failure
- 3. Nerve damage
- 4. Postop TMJ dysfunction
- 5. Postop infection
- 6. Postop sinus problems

Legal Involvement

- OMSNIC estimates **10-15%** of nerve-injured patients seek legal counsel



Lydiatt D. Litigation and the lingual nerve. JOMS 61: 197, 2003

- US jury verdicts, 1987-2000
- 33 suits in 12 states (42% California)
- Allegations
 - 52% lack of informed consent
 - 18% inadequate 3rd molar training
 - 15% wrong surgical approach
 - 12% failure to refer
- 58% defense verdicts, 39% plaintiff verdicts
- 3% settled (mean settlement: \$150,000)
- **Average award = \$306,737**

Diagnosis Caveats

- Spontaneous recovery occurs in **most** but not all patients
- Nerves in soft tissue (LN) have **lower** recovery rate than in bony canals (IAN)
- Documentation with **nerve testing** and **classification** is mandatory
- **Timely referral** for microsurgery provides best chance for recovery

Diagnosis Caveats

- Deficit **> 1 month** indicates high grade injury with uncertain recovery
- Continued improvement may be followed, but if improvement **stops**, it usually does not start again
- Most injuries resolve in **3-9 months**, but **only** if improvement began before **3 months**
- Patients anesthetic at **3 months** usually do not achieve recovery without microsurgery

Diagnosis Caveats

- Patients with sensation **that they find unacceptable** may be considered for microsurgery
- Microsurgical delay **decreases** success
- **Late** painful neuropathies are managed nonsurgically by a **neurologist**
- **Early pain** may indicate neuroma formation and warrant early surgery

Management Caveats

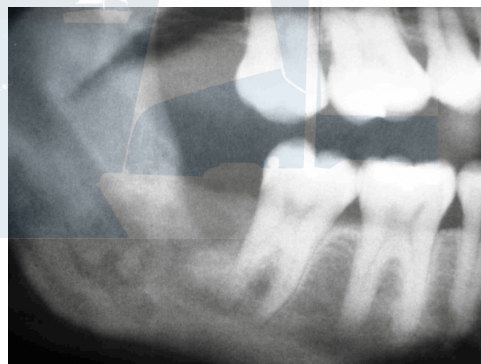
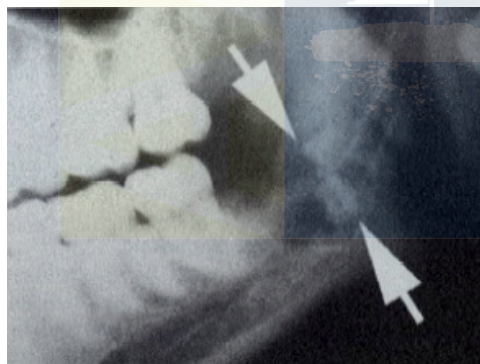
- A **timely referral** must be provided
- Angry, uninformed patients don't improve with any treatment
- Surgery at **3-6 months** is **more likely** to be successful than surgery **> 12 months**
- Surgery **may** improve **objective** function
- Surgery **may not** reduce **subjective** pain

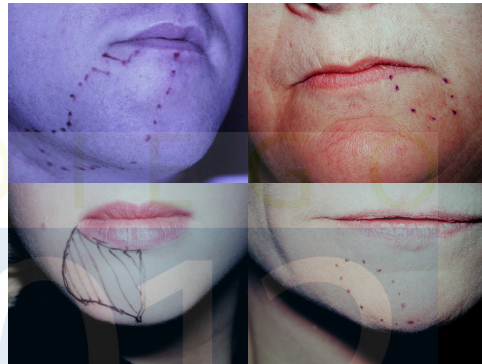
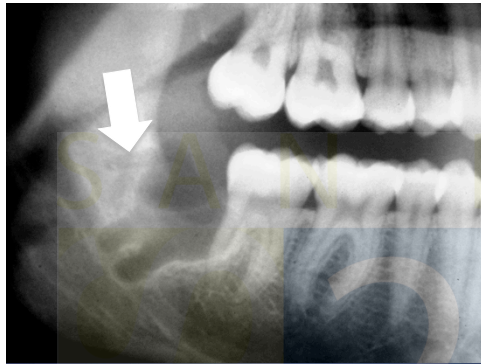
Medico-Legal "Damage Control"

- "My lip/tongue is still numb"
- **Surgeon** speaks with patient
 - Reassurance, recall preop discussions
 - Dictate details **now** (LA, flap, suture, nerve visualized) as **addendum**
 - Don't alter medical record
- Schedule follow-up (1-2 days)
 - Brief nerve exam (gross sensation)
 - Consider: **Medrol® dose-pak**
 - Sensory reeducation exercises

Medico-Legal "Damage Control"

- **1 week postop visit**
 - Nerve testing (light touch, two-point)
 - Subjective (VAS)
 - Panorax (retained root, foreign body)
 - Photographs for comparison?
- **1 month visit**
 - No change, or severe deficit: **referral**
 - Improvement, follow every 2 weeks





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Referral to Microsurgeon?

1. Observed nerve transection
2. Complete postop anesthesia ('unobserved' nerve injury)
3. No improvement at **1 month**
4. Residual subjective-only complaints
5. 2nd opinion to confirm OMS findings

Why Refer To Microsurgeon?

- Serial examinations by experienced surgeon
- Trial of medications
- Prompt microsurgery, if indicated

To Whom Do You Refer?

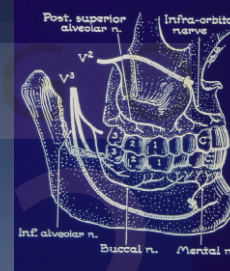
- Bruce Donoff, Boston, MA
- Salvatore Ruggiero, New Hyde Park, NY
- John Zuniga, Dallas, TX
- John Gregg, Blacksburg, VA
- Jim Green, Gainesville, FL
- Michael Miloro, Chicago, IL
- Tony Pogrel, San Francisco, CA
- **Regional Academic OMS Training Program**

Terminology

- **Paresthesia:** abnormal sensation, spontaneous or evoked, **no pain**
 - ↓ range: hypoesthesia to anesthesia
 - ↑ range: hyperesthesia to dysesthesia
- **Dysesthesia:** abnormal sensation, spontaneous or evoked, **unpleasant**
 - Hyperpathia, hyperalgesia
 - Causalgia : "burning pain"
 - Anesthesia dolorosa : pain in area of anesthesia
 - Allodynia : pain to non-painful stimulus
 - Neuralgia: pain in distribution of nerve

Etiology of Nerve Injury

- **3rd molar removal**
- Maxillofacial trauma
- Orthognathic surgery
- Dental implants
- Salivary gland surgery
- Pathology
- Preprosthetic surgery
- Endodontic treatment



Incidence of Nerve Injury

- **3rd molar surgery (1-5% overall)**
 - IAN: 0.26 - 8.4%
 - LN: 0.1 - 22.0%
- **Orthognathic surgery (SSO)**
 - IAN: 0.025 - 84.6%
 - LN: rare (screws)

Robert R. Frequency of nerve injuries after 3rd molar removal. JOMS 63: 732, 2005

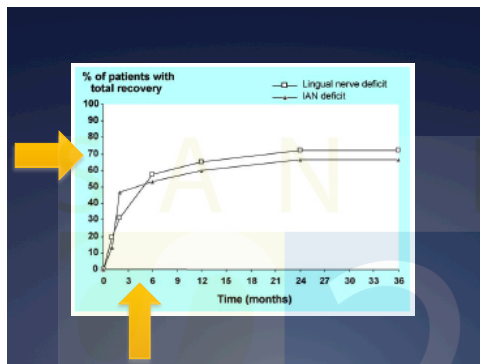
- Questionnaire to CAAOMS (n=535)
- 12 month period
 - 95% had an IAN injury, 53% had a LN injury
- In OMS lifetime of practice
 - 78% had a permanent IAN injury
 - 46% had a permanent LN injury
- **Temporary: IAN 0.4%, LN 0.1%**
- **Permanent: IAN 0.04%, LN 0.01%**
- Correlation with years of experience

Queral-Godoy E. Frequency of LN lesions after 3rd molars. JOMS 64: 402, 2006

- n = 4,995 lower 3rd molar extractions (Spain)
- **0.5% overall incidence of LN injury**
- 17 women, 6 men, mean age = 25.8 yrs
- 14 left, 10 right, 1 bilateral
- 100% had bone removal
- 20/24 had tooth sectioning
- Most recovered in 3 months

Cheung LK. Incidence of neurosensory deficits after 3rd molars. IJOMS 39: 320, 2010

- n = 4,338 cases
- 61% female, 39% male, ages 14-82
- **0.35% IAN deficit, 0.69% LN deficit**
- Most recovery occurs within 3-6 months
- LN risk: distoangular
- IAN risk: depth of impaction
- Experience is significant
- Not significant: sex, age, lingual flap, removal of distolingual bone, tooth sectioning



Jerjes W. Risk factors associated with injury to IAN and LN after 3rds, OOOE 109: 335, 2010

- n=3,236 patients
- 1 month
 - 1.5% IAN paresthesia
 - 1.8% LN paresthesia
- 24 months
 - 0.6% IAN
 - 1.1% LN
- IAN risks: age (26-30), horizontal impaction, radiographic proximity to IAC, trainee surgeon
- LN risks: males, distoangular impaction, radiographic proximity to IAC, trainee surgeons

3rd Molar Nerve Injury

Temporary

IAN
0.5-7.5%

LN
0.1-5.0%

Permanent

IAN
0.05-1.0%

LN
0.01-0.5%

Risk Factors For Nerve Injury

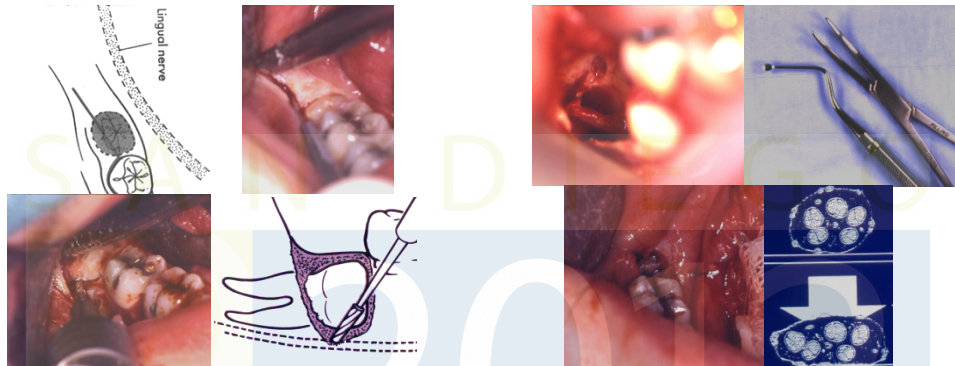
- Advanced age (>25 years)
- Female gender
- Depth of impaction
- Angulation (horizontal-IAN, distoangular-LN)
- Lingual orientation with loss of lingual cortex (LN)
- Bone removal, tooth sectioning
- Surgeon experience, duration of surgery
- Radiographic predictors

Female Predilection

- Pogrel MA. The etiology of altered sensation of the IAN, LN nerves as a result of dental treatment. J Calif Dent Assoc 27: 531, 1999
 - Female: Male = 3.3:1
- Coyle DE. Female rats are more susceptible to development of neuropathic pain using partial sciatic nerve ligation. Neurosci Lett 17: 186, 1995
 - Rat sciatic nerve ligation, measure paw withdrawal (allodynia)
 - 65% female, only 29% male, withdrew to non-noxious stimulus
 - Male rat nerves recovered better than female

3rd Molar Surgery Etiology

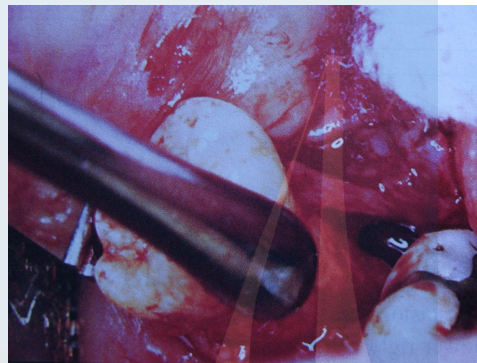
- LA injection
- Incision
- Flap reflection
- Bone removal
 - Lingual plate
 - IA canal
- Tooth sectioning
- Tooth elevation with nerve stretching
- Socket curettage
- "Follicle" removal
- Suture placement
- Dry socket medicaments



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Pogrel MA. Etiology of LN injuries in 3rd molar region. JOMS 64: 1790, 2006

- 16 cadaver LN injured, examined histologically
- 1. **Scalpel:** minimal fascicular damage, spontaneous recovery likely
- 2. **Hemostats:** crush injury, fascicular disruption, but limited extent, resection and early repair
- 3. **702 fissure bur:** ragged fascicular injury, delayed repair, possible graft
- 4. **Stretch > 120% of length:** diffuse fascicular disruption, delayed repair, graft likely



Radiology of the Nerve

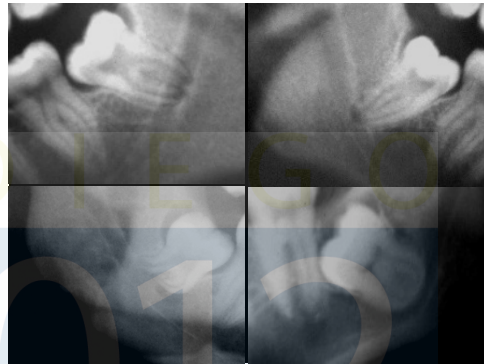
- A. To assess risk of nerve injury
 - Panorax
 - CT (limited use), 3DCT (cone-beam)
 - MRI
- B. To assess existing nerve injury
 - HR-MRI
 - MRN (magnetic resonance neurography)
 - Magnetic source imaging

**Miloro M, Kolokythas A.
Inferior alveolar and lingual
nerve imaging.
Atlas Oral Maxillofac Surg
Clin N Am 19: 35-46, 2011**

7 Panoramic Predictors of IAN Risk

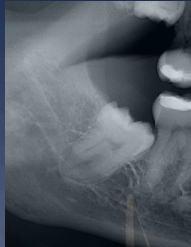
Rood JP, Sheehab BA. *Brit J Oral Maxillofac Surg* 28:20, 1990

1. Root Darkening
2. Root Deflection
3. Interruption of White Line of Canal
4. Root Narrowing
5. Dark & Bifid Root Apex
6. Canal Diversion
7. Canal Narrowing



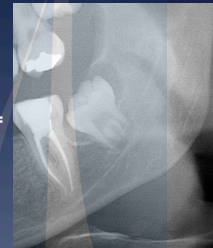
Howe GL, Poynton HG. Prevention of damage to IAN during extraction of 3rds. *Br Dental J* 109: 355, 1960

1. Root darkening (radiolucent band across the roots continuous with the white lines of IAC)
2. Interruption of white lines of IAC
3. Canal narrowing



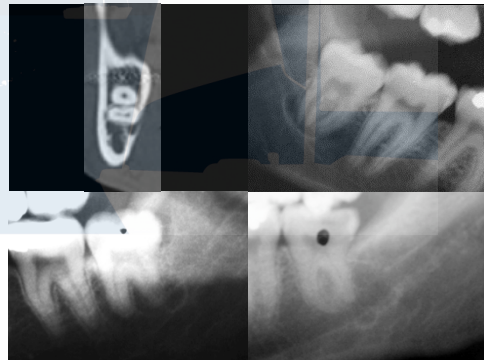
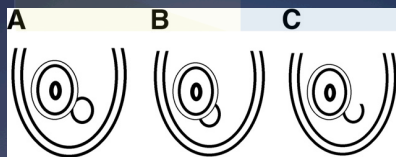
Radiographic Predictors

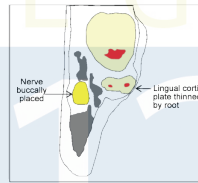
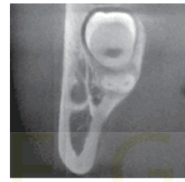
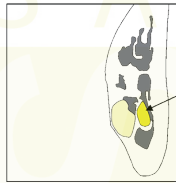
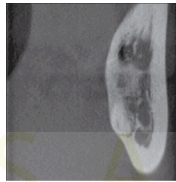
- Blaeser BF, August MA. Panoramic risk factors for IAN injury after 3rd molars. *JOMS* 61: 417, 2003
- No radiographic findings = minimal risk (<1%)
- 1 or more findings = increased risk (1.7-12%)



8th Radiographic Predictor

- Periapical radiolucency
- Loss of cortical integrity between IAC and root PDL space

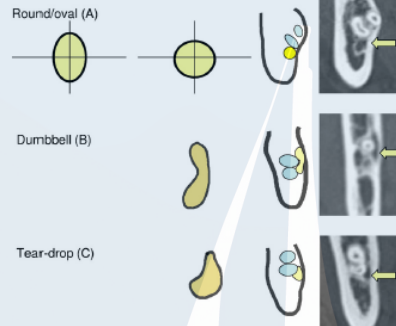




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Ueda M. Clinical significance of CT assessment and anatomic features of the IAC as risk factors for IAN injury at 3rd molar surgery. JOMS 70: 514, 2012

- 99 pts (145 teeth) CTs reviewed
- 3 canal shapes: round/oval, teardrop, dumbbell
- 7/145 IAN injuries (4.8%)
- All 7 lacked cortication
- 3/7 dumbbell, 4/7 round/oval

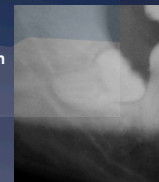


García, GS, Valmaseda-Castellón E, Gay-Escoda C. Does CT prevent IAN injuries caused by lower 3rd molar removal? JOMS 70: 5, 2011

- Retrospective cohort study of 150 extractions
- Most common indications for CBCT = patient age and Rood predictors on pano
- CT group (95) – pano + CT, Control (55) – pano
- 15 (10%) in CT, 6 (4%) in Control had IAN impairment
- Logistic regression models indicate that CBCT does **NOT** decrease risk of IAN injury

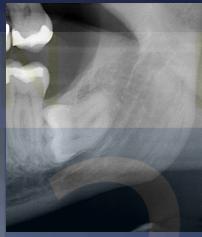
Miloro M. Radiographic proximity of 3rd molar to IAC. OOOOE 100: 545, 2005

- 560 lower 3^{rds} on panorex
- Tooth-to-canal distance
- Mean distance of erupted: 0.88 mm
- Unerupted (all below canal, **neg**)
 - Mesioangular: - 0.97 mm (**p<.05**)
 - Vertical: - 0.61 mm
 - Distoangular: - 0.31 mm
 - Horizontal: - 0.24 mm



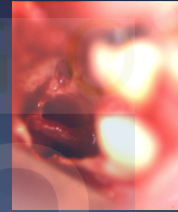
Miloro, OOOE 2005

- Temp IAN paresthesia = 3.33% (18)
- More common with **mesioangular** impactions (mean: -0.66 mm)
- More common in **females** (13/18)
- Mean age: 23.2 yrs



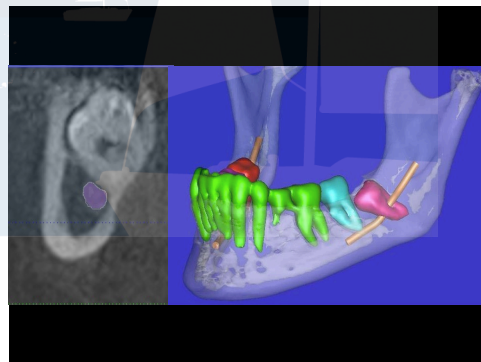
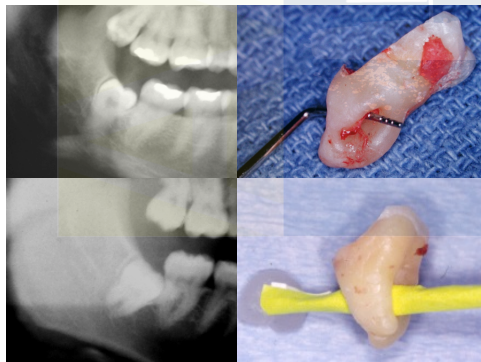
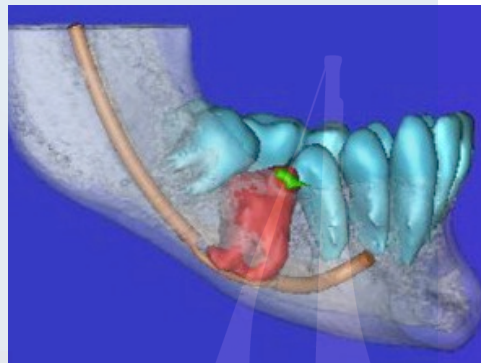
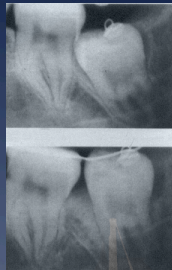
Tay ABG. Effect of exposed IAN during removal of 3rd molars. JOMS 62: 592, 2004

- n=192 nerves seen in 170 pts over 5 yrs
- 20% paresthesia @ 1 week
 - 58% recovered by 3 months
 - 65% recovered by 6 months
 - 71% recovered by 1 year
- 6% long-term paresthesia > 1 year



Forced Orthodontic Eruption

- Hirsch A. Use of orthodontic treatment to aid 3rd molar extraction: A method for prevention of nerve injury and improve periodontal status. J Periodontol 74: 1824, 2003
- n=18, 0% IAN injury
- Avg 2nd molar probing depths: 7.9 to 1.8 mm





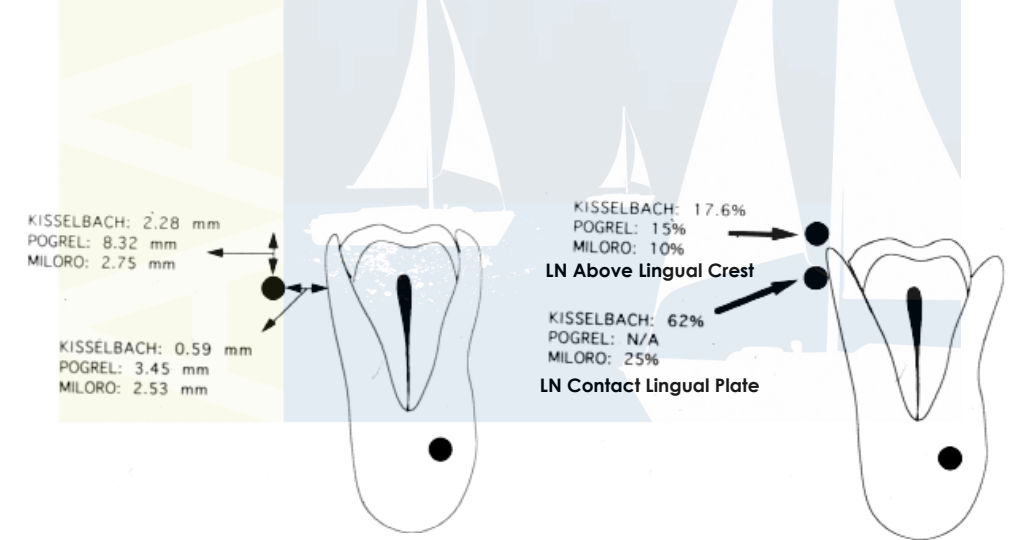
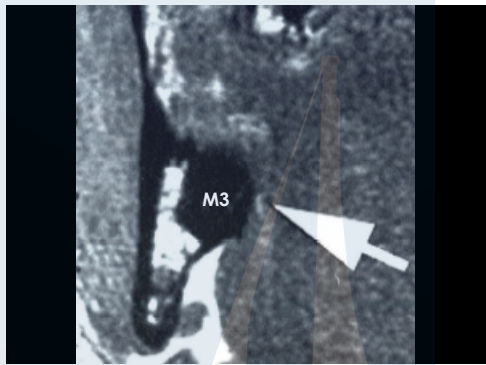
Lingual Nerve Position

Kisselbach, Chamberlain. Clinical and anatomic observations on relationship of lingual nerve to 3rd molar region. JOMS 42: 565, 1984

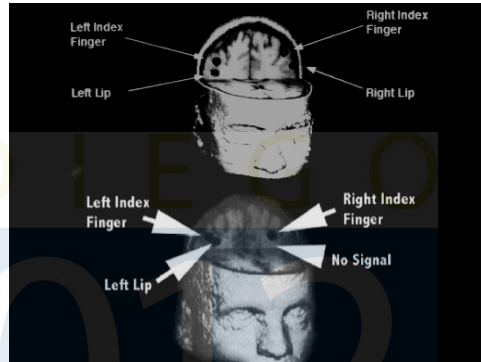
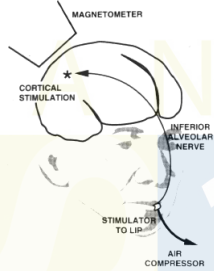
17.6% LN in soft tissue over impacted tooth

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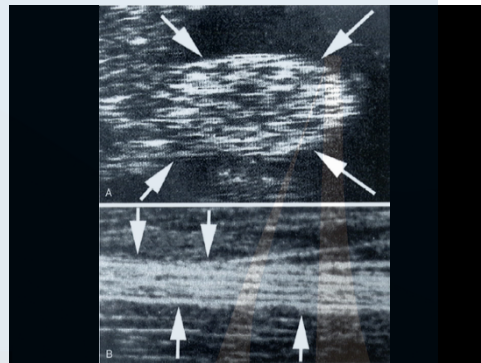
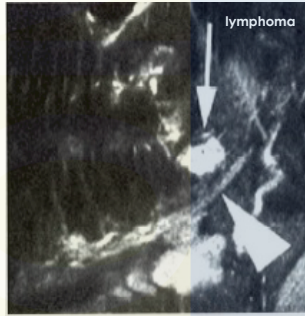
Miloro M. Assessment of LN in 3rd molar region using high-resolution MRI. JOMS 55: 134, 1997



McDonald, Pogrel. Noninvasive somatosensory monitoring of the injured IAN using Magnetic Source Imaging. JOMS 54: 1068, 1996

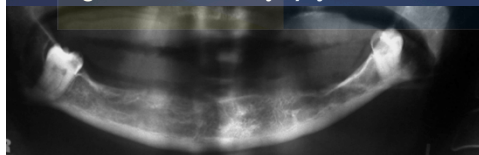


Filler AG. MRN. J Neurosurg 1996



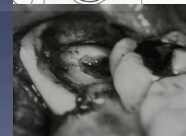
Coronectomy

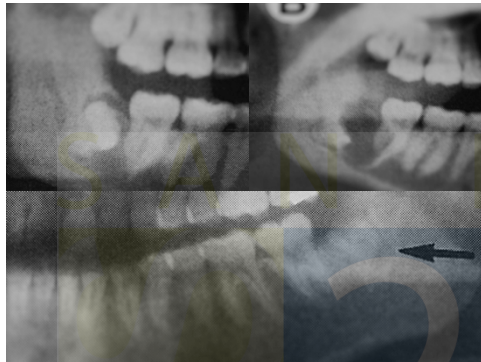
- Advanced age, mandibular atrophy
- Proximity to canal
- High risk of nerve injury, jaw fracture



Coronectomy

- 45 degree cut
- > 3mm below alveolar crest
- No pulp treatment
- Protect LN
- Not for horizontal impactions





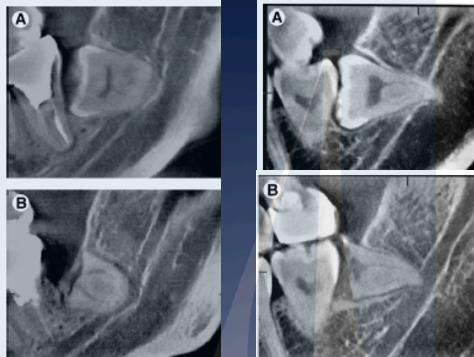
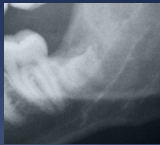
Coronectomy Literature

- O' Riordan BC. OOOO 98: 274, 2004
 - n=52 teeth in 10 yrs, 3 removed for infection, most roots migrate 2-3 mm, 1 pt (1.8%) IAN injury
- Pogrel MA. JOMS 62: 1447, 2004
 - n=50 teeth, 2 removed for infection (same pt), 1 for migration, 30% showed migration 2-3mm
- Renton T. Br J OMS 43: 7, 2005
 - n=128, 50/50 randomized extraction vs. coronectomy, 19% paresthesia with extractions, 0% with coronectomy, failed coronectomy (8%)

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Goto S. Clinical and dental CT evaluation 1 year after coronectomy. JOMS 70: 1023, 2012

- N=116 teeth (3/06-12/09)
- Only 1 root erupted into soft tissue
- 8 teeth extracted in 1-6 mos due to dehiscence
- No nerve injuries
- Average root migration = 3 mm
 - Females, <20 yrs age, conical roots



Risk Factors For LN Injury

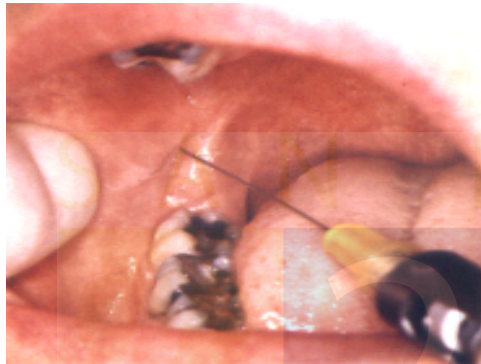
- Distoangular impaction
- Superficial position of LN
- Chronic pericoronitis
 - Scarring of LN toward surface
- Lingual version of tooth
 - Roots overlap 2nd molar roots
 - Missing lingual plate
- Right side (#32)
 - Right-handed surgeon can't see lingual region



Lingual Nerve Retraction Beirne, OOOO 91:395, 2001

- Review of 8 articles
- BA+ (buccal approach + LNR), BA- (BA - LNR), LS (lingual split + LNR)
- Temp: LS (9.6%), BA+ (6.4%), BA- (.6%)
- Perm: LS (.1%), BA+ (.6%), BA- (.2%)
- LNR: higher temporary, same permanent rates





Mandibular Block Injury

- Incidence?, unreported injuries
- Pagrel MA. Permanent nerve involvement resulting from IAN blocks. JADA 131: 901, 2000
 - n = 83 pts, 79% LN, 21% IAN
 - 36% dysesthesia
 - Estimate: 1:26,762-1:160,571
 - High incidence: 4% prilocaine



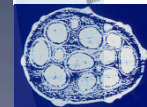
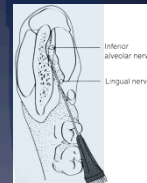
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Injection Injury Trends

- “Electric shock” on injection is uncommon
- High proportion of dysesthesia
- Non-anatomic pattern of nerve involvement
 - Demyelination to trigeminal ganglion
 - Adjacent nerve recruitment (V1V2)
- More common in females
- LN much more common than IAN

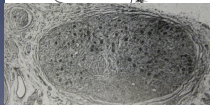
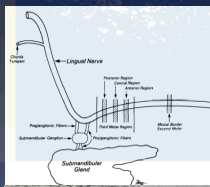
Why Lingual Nerve?

- Mouth opening stretches LN toward surface
- Multiple needle redirection
 - May cause direct injury, but no ‘shock’ since LN numb already
 - Less fascicles in 3rd molar region (3), more damage



Lingual N in 3rd Molar Region

- Smith E. Presence of nerve cell bodies in LN in 3rd molar area. JOMS 47: 931, 1989
- 44 cadaver halves
- 40/44 (91%) had cell bodies or ganglia along the LN in 3rd molar region
- Damage to cell body is IRREVERSIBLE vs. axonal injury



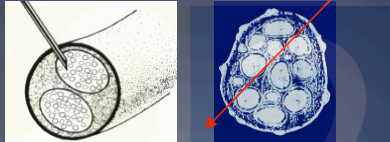
Block Injury Mechanisms

1. Direct neural trauma
 - Needle barb
 - Multiple redirections
2. Local anesthetic toxicity (%)
 - Epinephrine - local ischemia
3. Epineurial hematoma

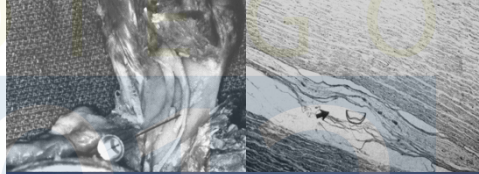


Direct Neural Trauma

- Occurs commonly but low % paresthesia
- If polyfascicular, trigeminal has interfascicular fissure
- If 1-3 fascicles, minor injury may have major effect
- May be 'needle barb' or 'multiple redirection' injury



Pogrel MA. Nerve damage associated with IAN blocks. JADA 126: 1150, 1995



Local Anesthetic Toxicity

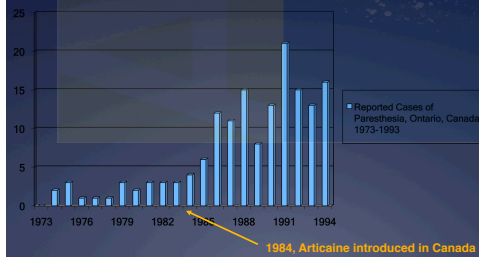
- More likely if intraneuronal
- Dysesthesia common
- 4% prilocaine > 2% lidocaine = 3% mepivacaine
- 4% articaine (concentration gradient)
 - Amide-ester combination
 - Contraindicated for blocks
- Epinephrine may exacerbate damage through ischemia



Haas DA, Lennon D. 21 year study of paresthesia after LA administration. J Can Dent Assoc 61: 319, 1995

- Ontario's prof liability program '73-'93
- n=143 injection injuries
- Age, gender, needle ga. not significant
- LN most frequently affected
- 1993: 14 cases of paresthesia-10 articaine 4%, 4 prilocaine 4%
- Paresthesia for 4% articaine (p<.002), 4% prilocaine (p<.025) greater than expected based on sales and distribution in 1993

Haas and Lennon, 1995



Frequency Distribution of Paresthesia 1993 Only

| Anesthetic | Total No. Cartridges Used | No. Paresthesias | Frequency % |
|--------------|---------------------------|------------------|-------------|
| Articaine | 4,398,970 | 10 | 71.4 |
| Bupivacaine | 241,679 | 0 | 0 |
| Lidocaine | 3,062,613 | 0 | 0 |
| Mepivacaine | 1,569,037 | 0 | 0 |
| Prilocaine | 2,352,615 | 4 | 28.9 |
| Total | 11,624,914 | 14 | 100 |

Frequency Distribution '73-'93

| Anesthetic | Frequency | Percentage |
|--------------|------------|------------|
| Articaine | 50 | 33.6 |
| Bupivacaine | 0 | 0 |
| Lidocaine | 5 | 3.4 |
| Mepivacaine | 4 | 2.7 |
| Prilocaine | 43 | 28.9 |
| Unknown (2+) | 47 | 31.5 |
| Total | 149 | 100 |

Garisto G, Haas DA. Occurrence of paresthesia after dental LA in the USA. JADA 141: 836, 2010

- 1997-2008 FDA Adverse Event Reports
- n=248, 95% mandibular blocks
- 89% LN
- Reports using 4% prilocaine (4% articaine) were 7.3 x (3.6 x) greater than expected based on use
- Caution: 4% solutions for mand blocks

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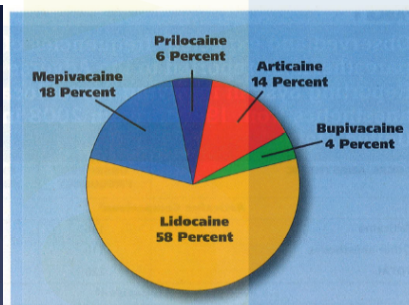
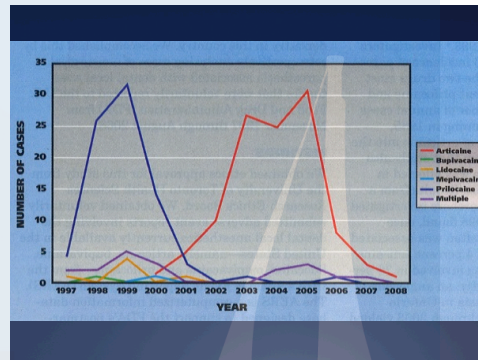


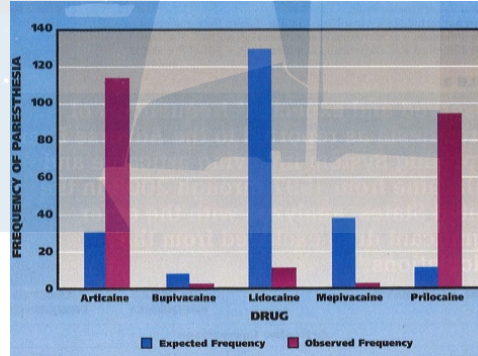
Figure 2. U.S. local anesthetic sales percentages from November 1997 through 2008. Source: Strategic Data Marketing, unpublished data, 2009.

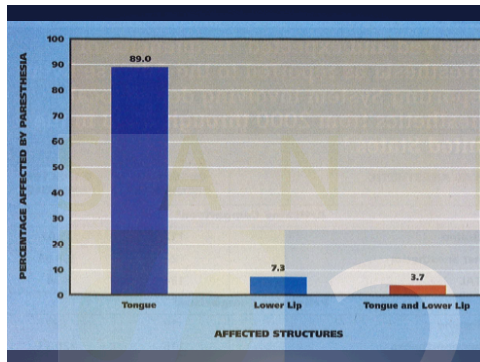


Observed and expected* frequencies of paresthesia as reported to the Adverse Event Reporting System involving dental local anesthetics from 1997 through 2008 in the United States.[†]

| LOCAL ANESTHETIC | OBSERVED FREQUENCY | EXPECTED FREQUENCY |
|--|--------------------|--------------------|
| Articaine Comparison[‡] | | |
| Articaine | 116 | 31.86 |
| Other anesthetics | 110 | 194.14 |
| TOTAL | 226 | 226 |
| Prilocaine Comparison[§] | | |
| Prilocaine | 97 | 13.26 |
| Other anesthetics | 129 | 212.74 |
| TOTAL | 226 | 226 |

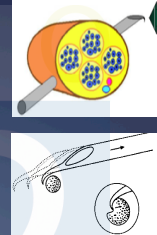
* Observed frequency: Number of cases. Expected frequency: Total number of cases x fractional use of specific drug.
[†] Does not include cases involving the use of more than one agent (n = 22).
[‡] The difference was statistically significant ($\chi^2 = 268.7, P < .0001$).
[§] The difference was statistically significant ($\chi^2 = 561.8, P < .0001$).





Stacy GC. Barbed needle paresthesias and trismus after dental regional anesthesia. OOOO 77: 585, 1994

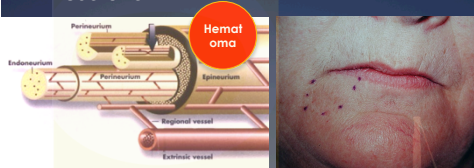
- A. n=100 27 ga. needles for IAN block examined microscopically
 - 60% had 'barbs'
- B. Pig model IAN block (n=90)
 - 80% had 'barbs'
 - Bevel toward operator (inward barbs)
 - Bevel facing away (outward barbs)
- C. Pig infraorbital nerve piercings
 - Outward barb worst fascicular injury



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Epineurial Hematoma Theory

- Transient, localized paresthesia from focal hematoma
- Lymphatic absorption, spontaneous resolution

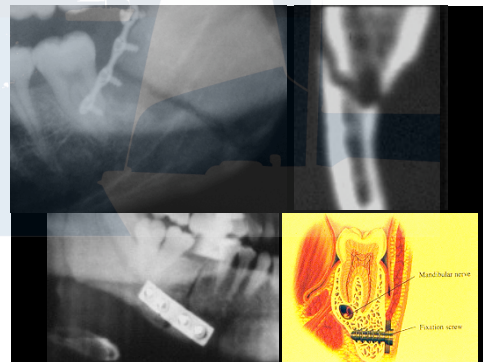
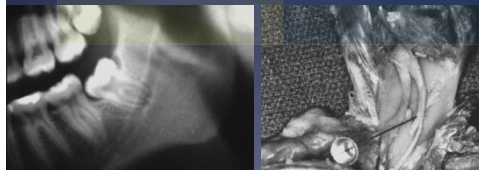


Injection Injury Prognosis

- 85% of cases resolve in 8 weeks
- Of the 15% that persist, less than 1/3 resolve completely
- No microneurosurgery (access)
- Drugs if dysesthesia

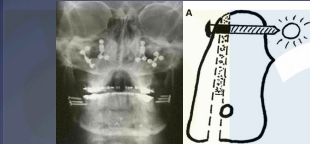
3rd Molar vs. Block Injury?

Pogrel. Trigeminal nerve chemical neurotrauma from injectable materials. OMFS Clin NA 2001



Orthognathic Surgery

- Zuniga J. **LN injury** as a complication of SSO. JOMS 48: 647, 1990
- Triplett G. **LN injury** due to overpenetration of bicortical screws for SSO. JOMS 54: 1451, 1996

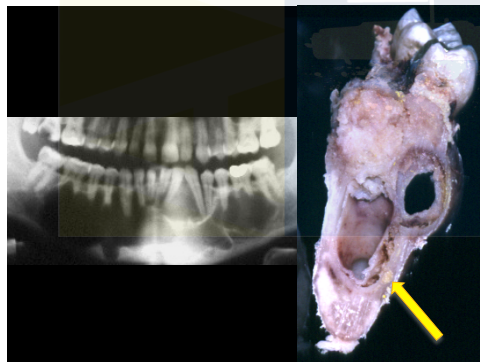
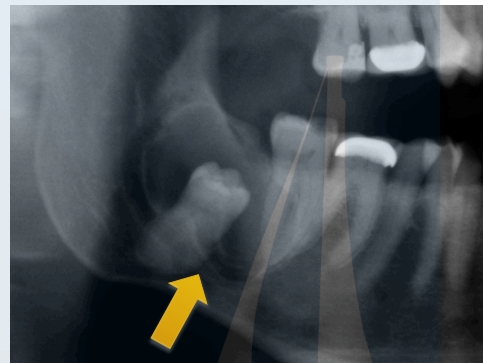


SSO Nerve Injury Risk Factors

1. Advanced age
2. Increased length of surgery, surgeon experience
3. Presence of 3rd molars
4. 'Bad splits'
5. Nerve manipulation
 - Medial retraction (decreased SSEPs)
 - Within osteotomy
6. Low corpus height (class II high MP angle)
7. Canal close to inferior border

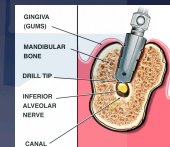
Al-Bishri. On neurosensory disturbance after SSO. JOMS 62: 1472, 2004

- n=43 questionnaires, > 1 yr after SSO
- 11.6% long-term subjective NSD
- Mostly women, over age 40
- **Corticosteroid use**
 - 15% with steroids reported long-term NSD
 - 30% without steroids
 - Not statistically significant



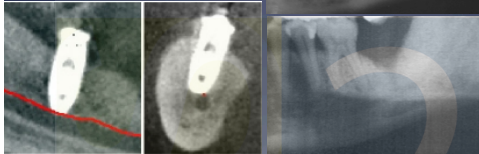
Dental Implants

- Nerve injury common
- Lack of literature
- No consensus on care
- Pilot drill through canal
- Compartment syndrome
 - Venous bleeding
 - Pressure in canal



Some Consensus

- Numb + implant in canal (panorex or CBCT) = implant removal, or shorter



No Consensus

- Numb + implant in canal = implant removal, or shorter
- Numb - implant in canal = Etiology? (block?)
- Observation
- Steroids
- Remove implant
- Shorter implant

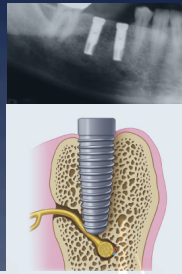
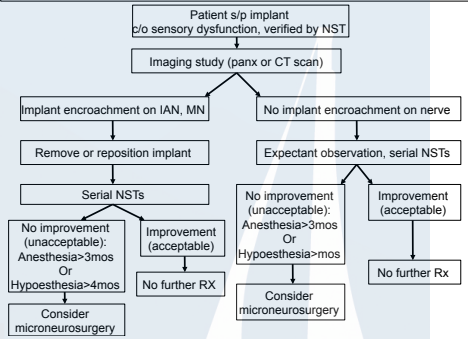


TABLE 1 : Algorithm for management of patient with paresthesia after implant placement.

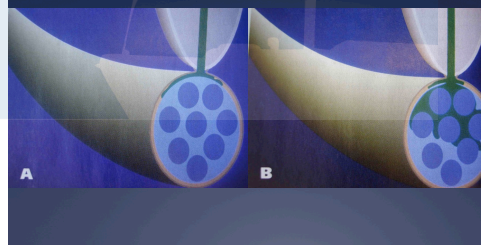


Nerve Repositioning

- Louis P. OMS Clinics of NA. May 2001
- 30-40% permanent altered sensation
- Advanced age

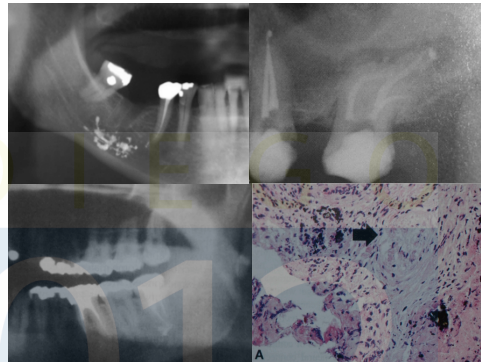


Endodontic Injury



Endodontic Nerve Injury

- A. Physical compression
- B. **Neurotoxicity**
 - Paraformaldehyde pastes
 - Sargenti, N2, AH26
 - Eugenol-containing cements
 - ZOE, PCS
- Prompt exploration and debridement (12-24 hrs)
- Scolozzi. Successful IAN decompression for dysesthesia following endodontic treatment. OOOO 97: 625, 2004



Chemical Injury

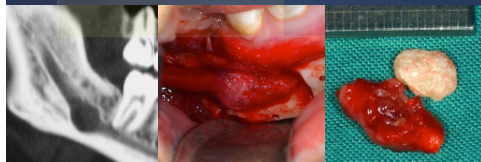
- Leist, Zuniga. Experimental topical **tetracycline**-induced neuritis in the rat. JOMS 53: 427, 1995
- Zuniga, Leist. Topical **tetracycline**-induced neuritis: A case report. JOMS 53: 196, 1995
- Caution: **terra-cotril** for dry socket

Chemical Injury

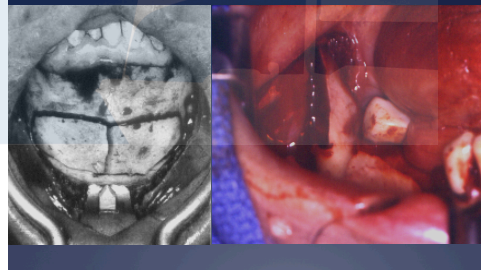
- Tetracycline: direct neurotoxicity
- Loescher, Robinson. Effects of surgical medicaments on peripheral nerve function. Br J OMS 36: 327, 1998
 - Rat saphenous nerve
 1. BIPP paste (bismuth iodoform paraffin): no effect
 2. Whitehead's varnish: some effect
 3. **Surgicel** (oxidized cellulose): acidic environment, potential neurotoxicity
 4. Carnoy's (FACE): < 5 min, reversible

Katre C. IAN damage caused by bone wax in 3rd molar. IJOMS 39: 511, 2010

- Developed paresthesia 11 years later after 3rds and bone wax



Intraoral Bone Graft Harvest



Distraction Osteogenesis

- Axoplasmic edema
- No fascicular injury
- Neurapraxia: transient conduction block
- Prompt recovery



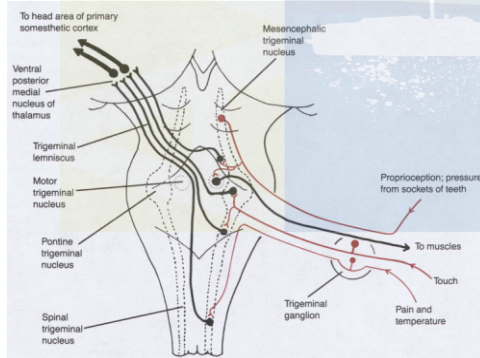
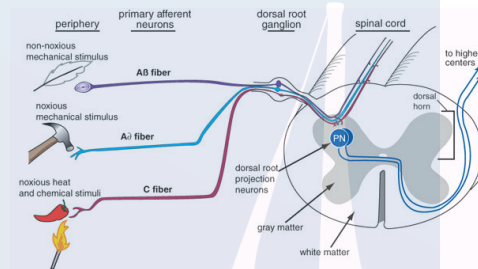
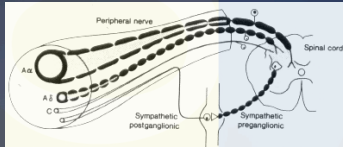
Meyer. Effect of DO on IAN function. JOMS 62: 292, 2004

- 5 advancements of 10-14 mm
- Age: 22-32 yrs, 4 F, 1M
- Testing: preop, postop, 7d, 3m, 6m, 9m, 12m
- **All 10 nerves normal by 12m**
 - 100% BSD
 - 4/10 S4+ (2PD = 2-6 mm)
 - 6/10 S3+ (2PD = 7-15mm)
 - 10/10 subjective hypoesthesia



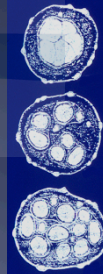
Trigeminal Nerve Anatomy

| Fiber Type | Size (μ) | Cond Vel (m/s) | Function |
|-----------------------|----------|----------------|---------------------|
| A-alpha (myelin) | 12-20 | 70-120 | Position/Fine Touch |
| A-beta (myelin) | 6.0-12 | 35-170 | Proprioception |
| A-delta (thin myelin) | 1.0-6.0 | 2.5-3.5 | Superficial Pain/T° |
| C (unmyelinated) | 0.5-1.0 | 0.7-1.5 | Deep Pain/T° |



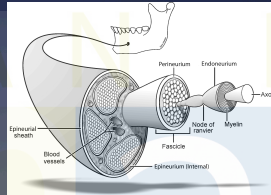
Fascicular Patterns

- Monofascicular (1 fascicle)
- Oligofascicular (2-10 fascicles)
- Polyfascicular (> 10 fascicles = Trigeminal)
- **LN in 3rd molar region may have fewer (1-3) fascicles**
- May explain paresthesia following minor trauma



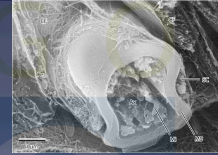
Trigeminal Nerve Anatomy

- Mesoneurium
- Epineurium
- Perineurium
- Endoneurium

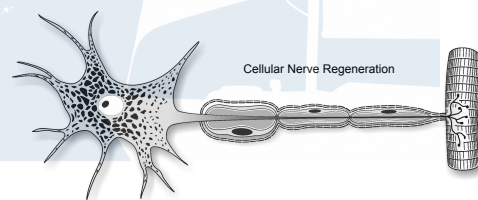
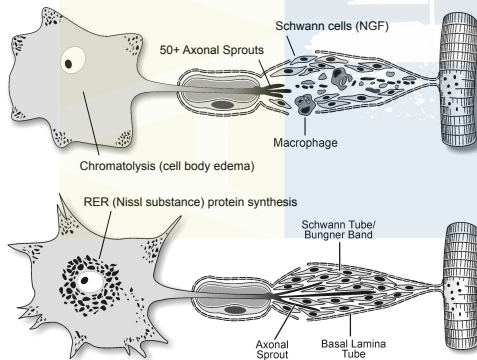
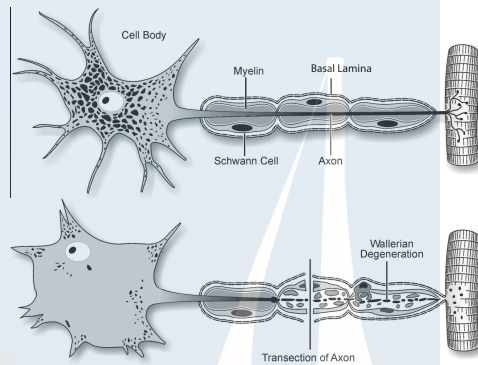
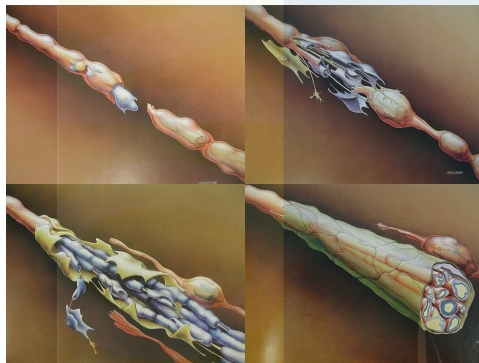


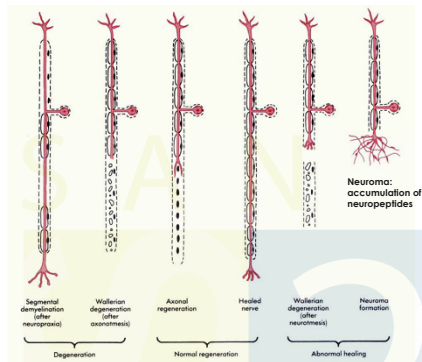
Nerve Healing

- Cellular regeneration
- Not tissue regeneration
- No nerve cell mitoses
- No increase in number of nerve cells, but axonal sprouting
- Neurotropic and neurotrophic factors



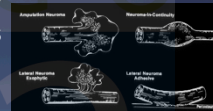
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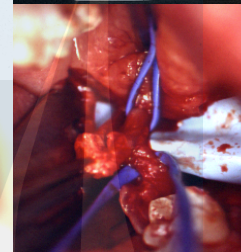
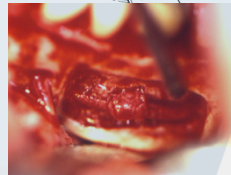
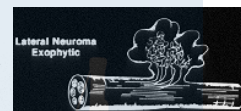
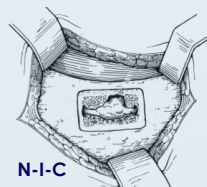
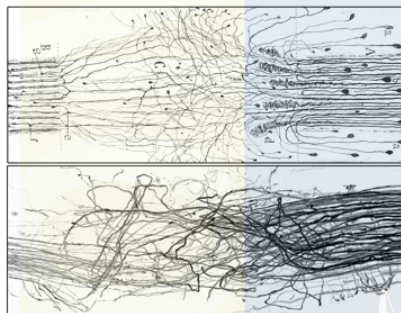


Neuroma Formation

- Amputation (stump) neuroma
- Neuroma-in-continuity (fusiform, central neuroma)
- Lateral neuromas
 - Exophytic-type
 - Adhesive-type



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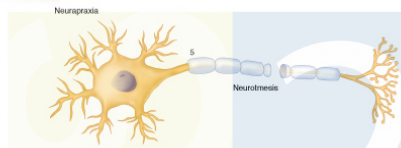
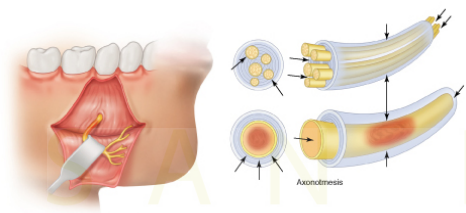
Patient Assessment

- History
- Clinical examination
 - Subjective (VAS)
 - Objective
 - Clinical neurosensory test
- Radiographs
- Nerve injury classification

Seddon Classification

- Seddon HJ, Three types of nerve injury. *Brain* 66:237, 1943
- Neurapraxia
- Axonotmesis
- Neurotmesis





Sunderland Classification

Sunderland S. A classification of peripheral nerve injuries produced by loss of function. Brain 74: 491, 1951

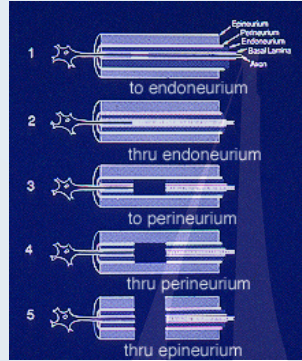
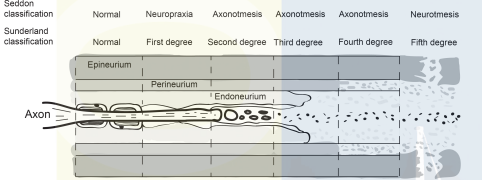
- First-degree Injury (Grade I)
 - Types I, II, III
- Second-degree Injury (Grade II)
- Third-degree Injury (Grade III)
- Fourth-degree Injury (Grade IV)
- Fifth-degree Injury (Grade V)



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Seddon vs. Sunderland

| | |
|-------------|-----------------------|
| Neurapraxia | Grade I (Types 1,2,3) |
| Axonotmesis | Grades II, III, IV |
| Neurotmesis | Grade V |



Sunderland vs. Recovery

| | Recovery | Rate of Recovery | Surgery |
|-----|-----------|------------------|---------|
| I | complete | fast (dys-wks) | - |
| II | complete | slow (wks) | - |
| III | variable | slow (wks-mos) | +/- |
| IV | poor/none | little/none | + |
| V | none | none | ++ |

History of Present Illness

- Etiology
- Onset of symptoms
- Progression of symptoms
- Any treatment (meds)
- Response to treatment
- Present symptoms

Visual Analog Scale

- 10 cm line, 5 degrees every 2.5 cm
- 1. Complete absence of sensation
- 2. Almost no sensation
- 3. Reduced sensation
- 4. Almost normal sensation
- 5. Fully normal sensation

1 2 3 4 5

Please indicate with an "X" on each of the two lines your perception of your current level of sensation.

| | 1 | 2 | 3 | 4 | 5 |
|-------|-------------------------------|---------------------|-------------------|-------------------------|------------------------|
| Right | Complete absence of sensation | Almost no sensation | Reduced sensation | Almost normal sensation | Fully normal sensation |
| Left | Complete absence of sensation | Almost no sensation | Reduced sensation | Almost normal sensation | Fully normal sensation |

FIGURE 41-6 Visual analog scale.

Clinical Examination

- Inspection
 - 3rd molar site
 - Lingual scar
 - Self-induced trauma
 - Atrophic papillae
- Palpation
 - Tinel's sign



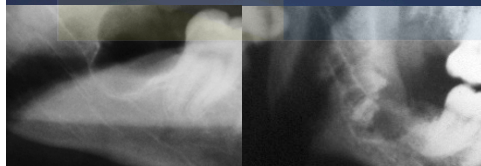
Tinel's Sign

- "Provocative test of regenerating nerve sprouts"
- Palpation of injury site elicits distal tingling sensation
- Sign of small fiber recovery
- Poorly correlated with functional recovery
- May be confused with neuroma



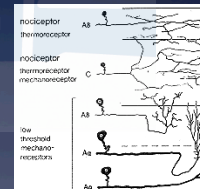
Post-Extraction Radiographs

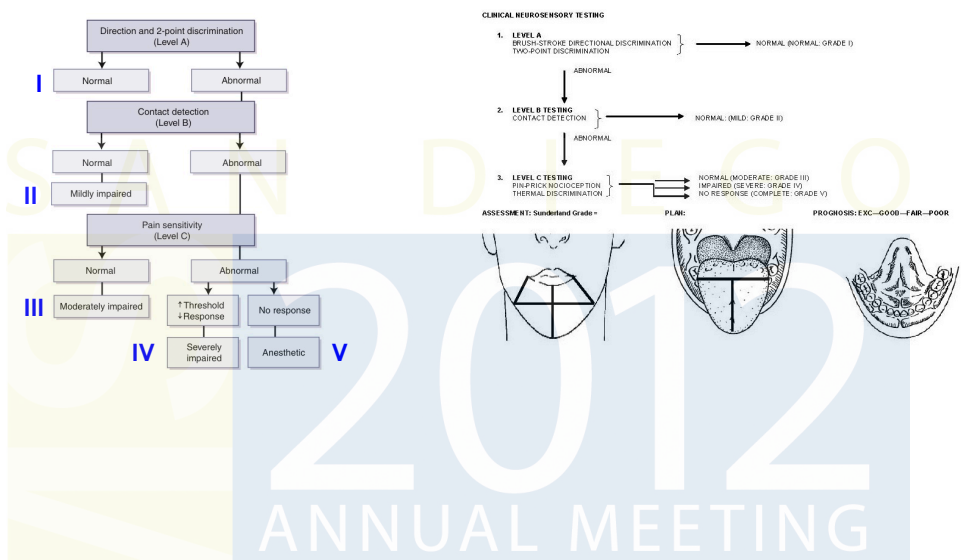
- To confirm presence of Rood predictors before bony healing
- Rule out roots, foreign body



Clinical Neurosensory Test

- Level A Testing
 - Brush stroke directional discrimination
 - Two-point discrimination
- Level B Testing
 - Contact detection
- Level C Testing
 - Pin prick nociception
 - Thermal discrimination



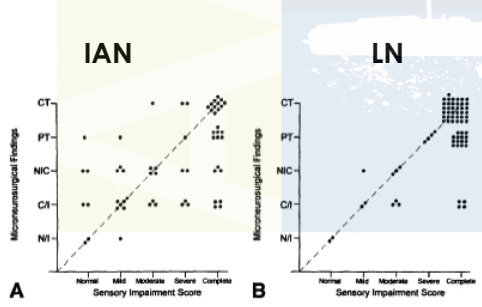


Zuniga, Meyer, Gregg, Miloro.
Accuracy of clinical neurosensory test for nerve injury diagnosis. JOMS 56: 2, 1998

- Multisite, randomized, prospective, blinded
- n = 130 patients: 60 IAN, 70 LN
- Clinical neurosensory test
 - Normal (I), Mild (II), Moderate (III), Severe (IV), Complete (V)
- Comparisons to nerve findings
 - Normal/intact (I), compressed/intact (II), N-I-C (III), partial transection (IV), complete transection (V)

JOMS 56: 2, 1998

| Preop Clinical NS Test | Surgical Findings |
|------------------------|--------------------------|
| Normal (I) | Normal/intact (I) |
| Mild (II) | Compressed/intact (II) |
| Moderate (III) | N-I-C (III) |
| Severe (IV) | Partial Transection (IV) |
| Complete (V) | Complete Transection (V) |

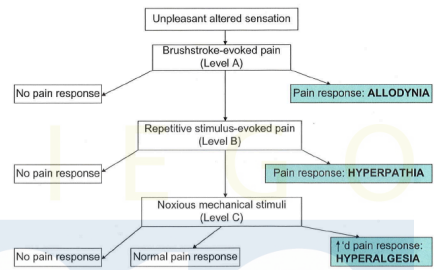


JOMS 56: 2, 1998

| | |
|---------------------------|--------------------------|
| IAN PPV = 77% | LN PPV = 95% |
| IAN NPV = 60% | LN NPV = 100% |
| IAN Sensitivity = 85% | LN Sensitivity = 100% |
| IAN Specificity = 47% | LN Specificity = 62.5% |
| IAN Accuracy = 68% | LN Accuracy = 96% |

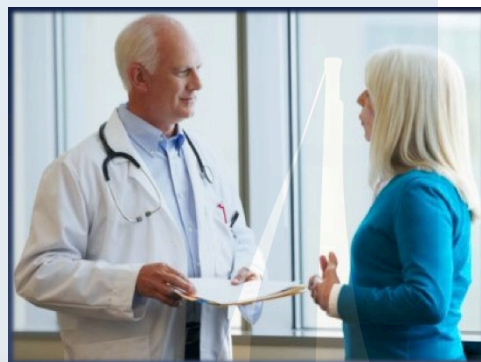
What about the evaluation of dysesthesia?

- Use same Levels A, B, C
- Increased subjectivity
- May be difficult to complete tests
- Most are Sunderland I or II with pain

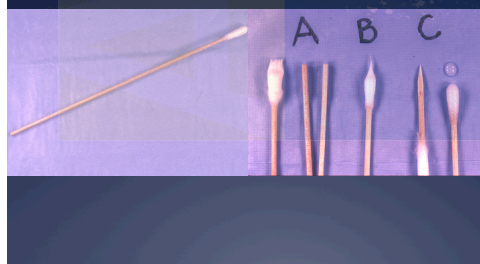


- Allodynia: pain due to a nonpainful stimulus
- Hyperpathia: increased reaction to a stimulus, esp. repetitive
- Hyperalgesia: increased response to a stimulus that is normally painful

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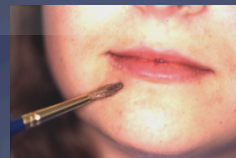


Clinical Neurosensory Testing



Brush Stroke Direction (Level A)

- Brush from R to L, L to R
- Number correct of 10: > 80% normal
- Alternate with control side

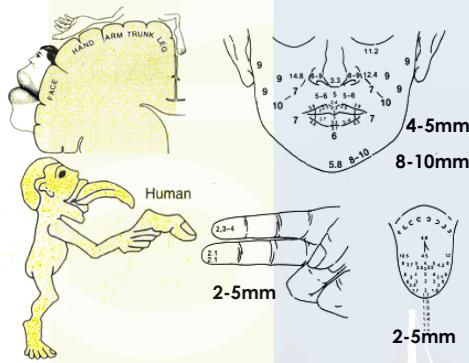


Two-Point Discrimination (Level A)

- Closest distance (mm) to discern 2 points
- Use blunt tips
- Compare to control side (Individual norms)



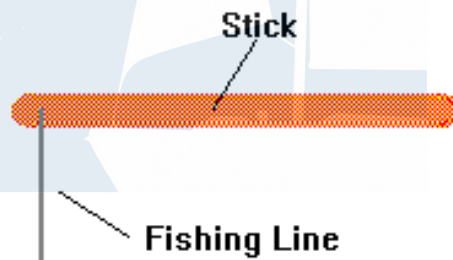
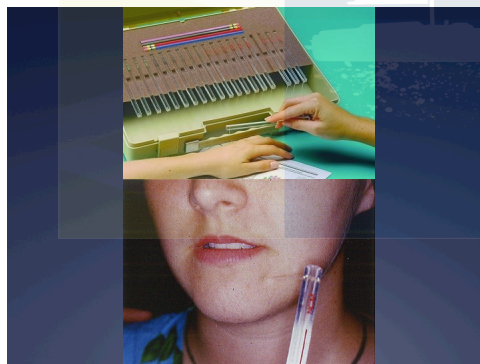
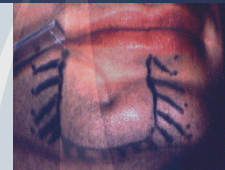
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Contact Detection (Level B)

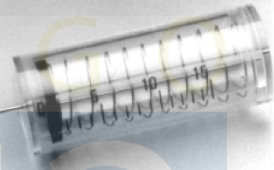
- Semmes-Weinstein monofilaments, "von Frey hairs"
- Acrylic rods with plastic fibers that bends with different pressures (gm of force)

| NORMAL - SEMMES-WEINSTEIN | | |
|---------------------------|------|------|
| 1.55 | 2.36 | 2.83 |
| 53 | 3 | 4 |
| 58 | 8 | 2 |
| 60 | - | - |
| 62 | 5 | 2 |
| n = 60 | | |



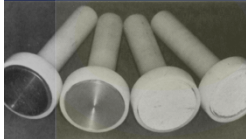
Pin Prick Nociception

- 30 ga. needle, all/none response

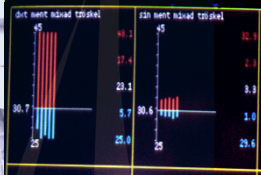
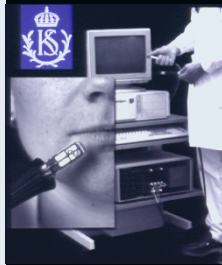


Thermal Discrimination

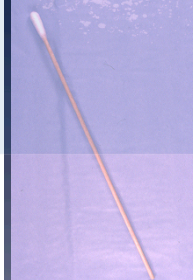
- Ice cold and hot water
- Minnesota thermal disks
- RollTemp® (25/40 deg C)



Thermotester®



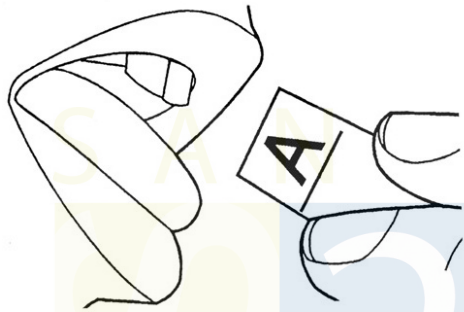
Thermal Discrimination



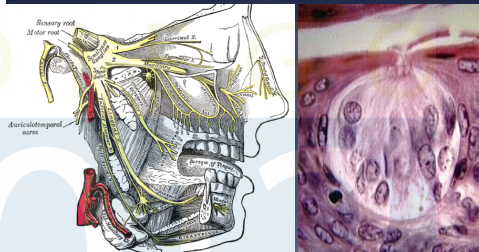
Stereognosis Testing

- Grids, Letters, Numbers
- van Boven domes

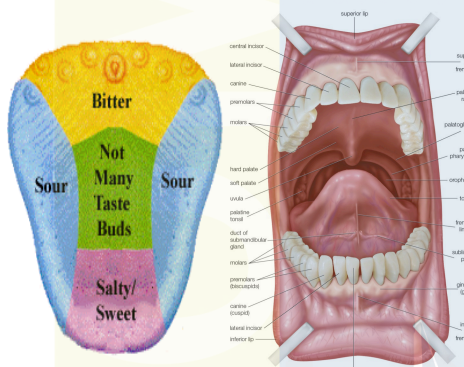




Taste Perception

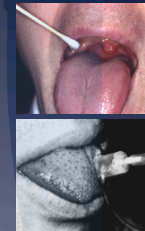


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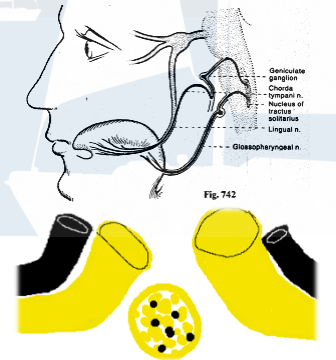
Clinical Taste Testing

- Whole-mouth taste testing
- Localized taste testing
- 1 M sodium chloride (salt)
- 1 M sucrose (sweet)
- 0.4 M acetic acid (sour)
- 0.1 M quinine (bitter)



Problems With Taste Testing

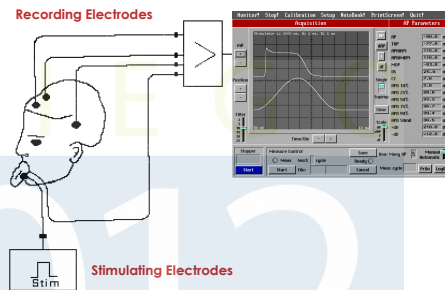
- Hillerup, S. Repair of LN after injury: Return of sensation and taste. JOMS 52: 1028, 1994
- Significant difference at 4 years of subjective and objective findings
- Wide variation in taste loss and recovery
- Poor correlation of taste (VII) and sensation (V3) recovery



Problem with “Objective Tests”

- Levels A, B, C (2PD, BSD, CD, Temp, PP) are “objective”
- Not objective since a patient response is “subjective”
- The only 100% objective test is SSEP

Somatosensory Evoked Potentials



This is a detailed dental examination form. It includes sections for 'Maxillary of Right' and 'Mandibular of Right' with diagrams of the teeth and tables for recording various dental procedures. The form also includes a patient photo and a 'Comments' section.

| Procedure | Code | Units | Units | Units |
|-----------|------|-------|-------|-------|
| Exam | 101 | 1 | 1 | 1 |
| Exam | 102 | 1 | 1 | 1 |
| Exam | 103 | 1 | 1 | 1 |
| Exam | 104 | 1 | 1 | 1 |
| Exam | 105 | 1 | 1 | 1 |
| Exam | 106 | 1 | 1 | 1 |
| Exam | 107 | 1 | 1 | 1 |
| Exam | 108 | 1 | 1 | 1 |
| Exam | 109 | 1 | 1 | 1 |
| Exam | 110 | 1 | 1 | 1 |
| Exam | 111 | 1 | 1 | 1 |
| Exam | 112 | 1 | 1 | 1 |
| Exam | 113 | 1 | 1 | 1 |
| Exam | 114 | 1 | 1 | 1 |
| Exam | 115 | 1 | 1 | 1 |
| Exam | 116 | 1 | 1 | 1 |
| Exam | 117 | 1 | 1 | 1 |
| Exam | 118 | 1 | 1 | 1 |
| Exam | 119 | 1 | 1 | 1 |
| Exam | 120 | 1 | 1 | 1 |

Management Options

- Observation
- Nonsurgical (drugs)
- Low-level (soft) laser therapy
- Sensory re-education exercises
- Microsurgery



Trigeminal Nerve Disorders Management

Michael Miloro, D.M.D., M.D., F.A.C.S.

Professor

Department Head & Program Director

Oral & Maxillofacial Surgery

University of Illinois at Chicago

Chicago, Illinois

Treatment Planning Considerations

- Sunderland grade I, II, III, IV, V
- Observed vs. unobserved injury
- Time from injury to repair
- Mechanism of injury
- Presence of dysesthesia
- ASA physical status

Nerve Injury Treatment Planning

- **Increased sensation**
 - Drugs
- **Decreased sensation**
 - Wait
- **Anesthesia = surgery**
 - IN in 1-3 months
 - IAN in 3-6 months



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Clinical Scenarios

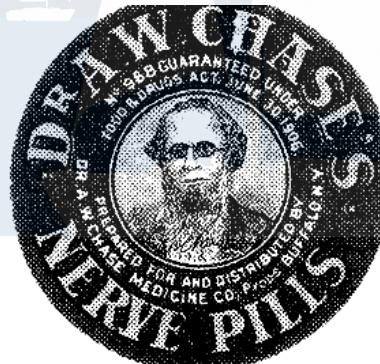
- **Nonpainful anesthesia**
- **Painful anesthesia (anesthesia dolorosa)**
- **Nonpainful hypoesthesia**
- **Painful hypoesthesia**
- **Nonpainful hyperesthesia**
- **Painful hyperesthesia**
- **Surgery**
- **Drug Therapy**

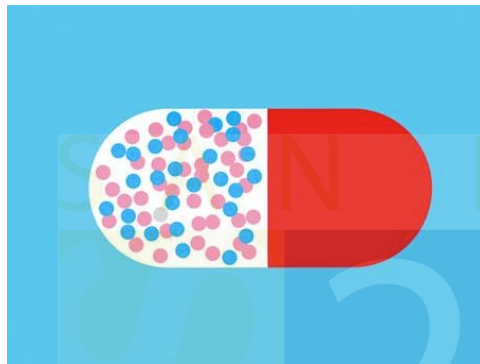
The Hypoesthetic Patient

- Etiology
 - 3rds, SSO, needle-stick
- Neurosensory testing
 - Should be < 50% for surgery
 - Successful improvement: 80-85%
- Time from injury to repair
 - Lingual: 3 months
 - IAN: 3-6 months
 - Or: no improvement in 1 month

The Dysesthetic Patient

- Etiology
 - 3rds, needle-stick, SSO-rare
 - Implant: removal?
- Neurosensory testing
 - Usually 90-100%, microsurgery not indicated
- Time from injury to repair
 - Early (< 6 months): drugs, consider microsurgery for neuroma
 - Late (> 6 months): drugs





Pharmacotherapy for Neuropathic Pain

- **1. Membrane stabilizing drugs to prevent ectopic neural discharges**
 - Antidepressants, anticonvulsants
 - Elavil, dilantin
- **2. Dorsal horn inhibitors (GABA agonists)**
 - Muscle relaxants, benzodiazepines
 - Neurontin
- **3. Topical agents**

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Pharmacotherapy

- Local anesthetic nerve blocks
- Corticosteroids (medrol dose-pak)
- B-complex vitamins (B1, B6, B12)
- NSAIDs (ibuprofen, tylenol)
- Antidepressants
 - Tricyclics: amitriptyline (elavil)
 - Tetracyclics: doxepin (sinequan)
 - Serotonin antagonists: fluoxetine (prozac) and duloxetine (cymbalta)

Pharmacotherapy

- Anticonvulsants
 - Phenytoin (dilantin)
 - Carbamazepine (tegretol)
 - Gabapentin (neurontin)
 - Levetiracetam (lyrica)
 - Levetiracetam (keppra)
- Muscle relaxants: baclofen (lioresal)
- Benzodiazepines: clonazepam (klonopin)
- Antisymphathetics (SMP)
 - Propranolol, guanethidine, phenoxybenzamine, prazosin, clonidine

Pharmacologic Therapy

- Topical crèmes: capsaicin (zostrix)
- Eutectic mixtures of topical crèmes
 - Ketoprofen 10%/tegretol 2%/lidocaine 10%
 - Elavil 2%/capsaicin .075%/lidocaine 5%/clonidine .2%
 - Ketoprofen 10%/guaifenesin 10%/capsaicin .075%/lidocaine 4%
 - Neurontin 6%/clonidine .02%
 - Ketoprofen 10%/baclofen 5%/lidocaine 5%
 - Ketamine 10%/neurontin 6%/clonidine .2%

Current Pharmacologic Options

- **Neurologist consultation**
- Steroids, B-complex vitamins
- Capsaicin crème 0.075% HP tid
- Neurontin (gabapentin) 300 mg tid
- Lyrica (pregabalin) 100 mg tid
- Baclofen (lioresal) 10 mg tid
- Clonopin (clonazepam) 1.0 mg tid
- Elavil (nortriptyline) 25 mg tid

Corticosteroids

- Evidence to support use, spinal cord injury, orthognathics (SSO)
- Decrease perineurial edema, especially in immediate postoperative period
- Medrol Dose-Pak (contains 21 4 mg pills)
 - Methylprednisolone 4 mg
 - Begin with 6 pills (24 mg)
 - Take one less each day for 6 days



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B-Complex (B1/B6/B12) Vitamins

- B1 (thiamine), B6 (pyridoxine), B12 (cyanocobalamin)
- Analgesic role in neuropathic pain
- Rat studies show benefit in experimental hyperalgesia (spinal cord compression)
 - Song, *Anesthesiology*, 2009
 - Wang, *Pain*, 2005



Acetyl-L-carnitine (ALCAR)

- Amino acid nutritional supplement
- Alzheimer's disease
- *Wilson A. Acetyl-L-carnitine increases nerve regeneration and target organ reinnervation. JPRAS 63: 1186, 2010*
- Rat sciatic nerve model
- ALCAR 50 mg/kg/day IV
- Increased number of regenerating nerve fibers and target organ reinnervation (gastrocnemius muscle bulk)



Capsaicin Crème (Zostrix)

- Chili pepper extract
 - Chew chili peppers
- Decreases substance P
- Apply to area tid prn
- Skin, mucosa irritation
- 0.025% LP, 0.075% HP

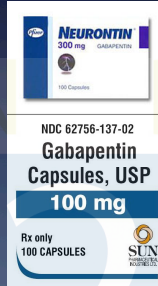


Capsaicin Crème



Gabapentin (Neurontin)

- Anti-epileptic drug
- Exact mechanism unknown
- Mimics GABA (inhibitory neurotransmitter)
- Begin 300 mg po tid, then taper
 - 200/300/300, 200/200/300, 200/200/200, 100/200/200, 100/100/200, 100/100/100, ...
- Max: 3600 mg/day
- Side effects: mild drowsiness



Lyrica (Pregabalin)

- Anti-epileptic drug
- For fibromyalgia
- Similar mechanism to gabapentin
- Used for DM neuropathy
- Increases GABA (inhibitory)
- 75-100 mg po tid (max: 600 mg/day)



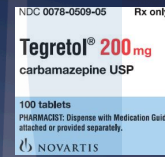
Keppra (Levetiracetam)

- Anti-epileptic drug
- Used for partial seizures
- 500 mg po bid
- Max: 3000 mg/day



Carbamazepine (Tegretol)

- Anti-convulsant drug
- 100-300 mg po tid
- Therapeutic dose: 900-1200 mg/dl
- Monitor blood levels: 4-12 mcg/ml
- Hepatotoxicity (LFT)
- Agranulocytosis (CBC)
- No longer a first-line agent



Clonazepam (Klonopin)

- Benzodiazepine (GABA_A agonist)
- Suppresses spike and wave seizure foci
- 1.0 mg po tid
- Maximum dose: 20 mg/day



Amitriptyline (Elavil)

- Antidepressant
- Blocks 5-HT and NE reuptake
- 50 mg po qhs
- Max: 300 mg/day



Other Methods

- Classically for trigeminal neuralgia
- Nerve injections
 - Alcohol
 - Glycerol
- Radiofrequency thermal neurolysis
- Cryotherapy

Other Methods

- Gregg JM, Small EW. Surgical management of trigeminal pain with radiofrequency lesions of peripheral nerves. JOMS 44: 122, 1986.
 - 68% recurrence of pain at one year
- Fardy MJ, Patton DW. Complications associated with peripheral alcohol injections in the management of trigeminal neuralgia. Brit J OMS 32: 387, 1994.

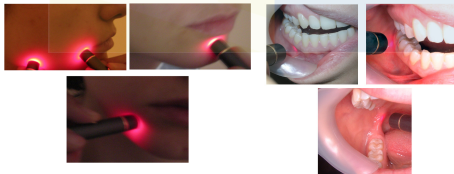
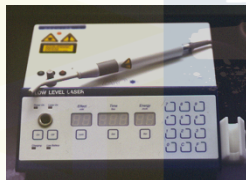


Low Level Laser ("Soft Laser")

- Wound healing capabilities (all tissues)
- Direct effect on injured axons and NGF production
- Mechanism: rhodopsin-kinase enzyme
 - Active at 820nm wavelength (Ga-Al-Ar)
 - NF-kappa B translocation into nucleus
 - Transcription of neural repair elements
- No FDA approval, yet

LLL Nerve Studies

- Khullar. Effect of LLL on neurosensory deficits subsequent to SSO. OOOO 82: 132, 1996
- Khullar. Preliminary study of LLL for treatment of long-standing (> 2 years) sensory aberrations of the IAN. JOMS 54: 2, 1996



Miloro M. LLL effect on neurosensory recovery after SSO. OOOO 89: 2000

- n=6 BSSO
- Bilateral LLL 6.0 joules x 4 sites
- Preop, 6 hrs, 24 hrs, days 2, 3, 4, 7
- CNT and VAS: preop, 6 hrs, 24 hrs, days 2, 3, 4, 7, 14, 28, 56

Miloro, 2000

- BSD normal by 2 weeks
- 2PD and CD normal by 8 weeks
- Temp and PP minimally affected, but remained deficient at 2 months
- VAS
 - 50% reported deficit at 2 days
 - Only 15% deficit at 8 weeks

Microneurosurgery Indications

- Complete anesthesia (0%)
- Less than 50% residual sensation
 - Sunderland III, IV, V
- Observed nerve transection
- **Early** dysesthesia (neuroma formation)

Microsurgery Not Indicated

- Sensation improves at each visit
- **Late** dysesthesia (esp IAN)
- Other contraindications
 - Anesthesia dolorosa
 - Sympathetic-mediated pain (CRPS)
 - Complex regional pain syndrome
 - Deafferentation pain
 - Trigeminal neuralgia
 - Atypical facial pain

AAOMS Nerve CIG, 1996

- Microsurgery, when indicated should be considered (time after injury):
 - **Lingual Nerve** 1-3 months
 - **Inferior Alveolar Nerve** 3-6 months

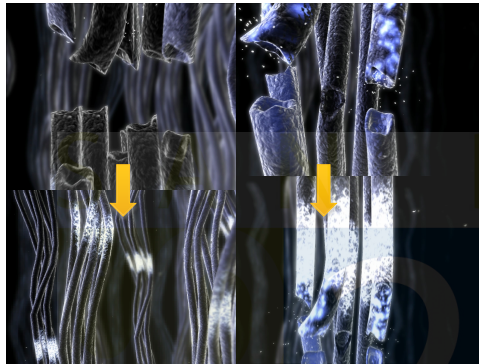
Unobserved Injury Algorithm

- Monitor with clinical NS testing
- If 0-50% sensation:
 - LN repair: 1-3 months
 - IAN repair: 3-6 months

Observed Injury Algorithm

- Sunderland I, II, III (nerve visualized)
 - Clinical NS testing, surgery if indicated
- Compression (root, implant, jaw fracture)
 - Immediate decompression
- Chemical (RCT, tetracycline)
 - Immediate debridement
- Sunderland IV, V
 - Clean: immediate repair
 - Avulsive: delayed primary repair (21d)





Meyer RA, AAOMS, Chicago, 1991

- Success after repair of severed IAN, LN nerves
- 90% if repaired by 3 months
- 80% if repaired by 6 months
- 10% if repaired at 12 months

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Why Does Time Matter?

1. Pons. Massive **cortical reorganization** after sensory deafferentation in adult macaques. *Science* 252: 1159, 1991
2. Zuniga. **Trigeminal ganglion cell** response to mental nerve section in the rat. *JOMS* 57: 427, 1999
3. Waller. **Distal nerve degeneration** following injury. *Britt Med J* 1892

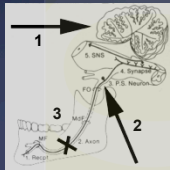


Table 1. STEREOLOGICAL MEANS IN THE MANDIBULAR SUBDIVISION OF THE TRIGEMINAL GANGLION

| Groups* | N | V _{ref} (mm ³) | N _v (×10 ³ μm ⁻³) | N (×10 ³) |
|-----------------|----|-------------------------------------|---|-----------------------|
| Sham surgery | 12 | 3 (.05)† | 3.53 (.29)‡ | 20.6 (2.9)‡ |
| 90 POD | 6 | 3 (.06)† | 3.65 (.35)‡ | 20.9 (3.5)‡ |
| 180 POD | 6 | 31 (.04)† | 3.3 (.09)‡ | 20.2 (1.65)‡ |
| Axotomy surgery | 12 | 22 (.04)† | 2.2 (.09)‡ | 10.88 (.92)‡ |
| 90 POD | 6 | 21 (.06)† | 2.36 (.19)‡ | 11.17 (1.13)‡ |
| 180 POD | 6 | 22 (.05)† | 2.09 (.15)‡ | 10.6 (.74)‡ |

Published Success of Microsurgery

- 30-50% "success"
- Not standardized
 - Few multicenter trials (1 surgeon)
 - Patient age
 - Etiology of injury
 - Delay from injury to repair
 - Surgical technique
 - Clinical NS exam
 - Follow-up period
 - "Success" criteria



Leung YY. Treatment modalities of neurosensory deficit after lower third molar surgery: A systematic review. *JOMS* 70: 768, 2012.

- Systematic literature review identified 10 articles (of 1112 returned)
- 4 surgical, 2 nonsurgical options
- Total surgical: 166 LN, 23 IAN
- Total nonsurgical: 14 LN, 32 IAN
- "Significant improvement" in surgical ranged from 25-66.7%
- Acupuncture and low-level laser showed "significant improvement" in >50%
- Any treatment option rarely produces complete recovery
- Timing too variable to determine optimal repair time
- No standardized assessment criteria for success

Leung, 2012

| Treatment | Study | Nerve, n | Outcomes (Complete, Significant, Some Improvement, No Improvement) | |
|---------------------|--|-------------------|--|---|
| External neurectomy | Hillerup, 2007 | LN, 12 | 25-25-25-25 | |
| | Joshi, 2002 | IAN, 7 | 29-0-29-43 | |
| Direct suturing | Hillerup, 2007; Chen, 1997; Farole, 2008; Robinson, 2000 | LN, 87 IAN, 3 | 6-55-29-10 0-33-33-33 | |
| | Vein graft | Pogrel, 2001 | LN, 14 IAN, 14 | LN defect < 5mm: 0-33-67-0 LN defect > 5 mm: 0-0-0-0 IAN defect < 5 mm: 0-67-33-0 IAN defect > 5 mm: 0-33-67-0 |
| | Gore-Tex Tube | Pogrel, 1998 | LN, 21 IAN, 21 | 0-33-0-67 50-0-0-50 |
| Acupuncture | Ka, 2006 (Japanese) | LN, 12 IAN, 12 | 33-17-50-0 15-30-37-44 | |
| LLLT | Midamba, Haanes, 1993 | LN, 22 IAN, 22 | 13-75-13-0 25-5-25-0 | |

Normal Recovery Stages Following Sensory Trigeminal Nerve Injury (Mackinnon SE, 1988)

- Stage 0. No sensibility or response in primary injury zone
- Stage 1. Recovery of deep pain sense & response
- Stage 1+. Recovery of superficial pain sense & response
- Stage 2. Recovery of superficial pain & crude touch sense
- Stage 2+. Stage 2 with over-response
- Stage 3. Recovery of pain, abn touch with no over-response
- Stage 4. Complete recovery of control level sense, response
- Stage 5. Control level sense-responses, subjective normality

Table 1. MEDICAL RESEARCH COUNCIL SYSTEM FOR GRADING NERVE RECOVERY²⁴

| Grade | Description |
|-------------------------|--|
| Motor recovery | |
| M0 | No contraction |
| M1 | Return of perceptible contraction in proximal muscles |
| M2 | Return of perceptible contraction in proximal and distal muscles |
| M3 | Return of function in proximal and distal muscles to such a degree that all important muscles are sufficiently powerful to act against gravity |
| M4 | All muscles act against strong resistance, and some independent movements are possible |
| M5 | Full recovery of all muscles |
| Sensory recovery | |
| S0 | No recovery |
| S1 | Recovery of deep cutaneous pain |
| S1+ | Recovery of superficial pain |
| S2 | Recovery of superficial pain and some touch |
| S2+ | As in S2, but with over response |
| S3 | Recovery of pain and touch sensibility with disappearance of over response |
| S3+ | As in S3, but localization of the stimulus is good, and there is imperfect recovery of 3-point discrimination |
| S4 | Complete recovery |

Pogrel MA. Results of repair of IAN and LN. JOMS, 2000

- 1994-1999, n=880 patients
- 51/880 (6%) had surgery: 34LN, 17IAN
- Direct repair: 16LN, 10IAN
- Graft repair: 13LN, 7IAN (16 vein, 2 nerve, 2 gore-tex)
- 10 "good improvement" (1 normal)
- 18 "some improvement"
- 22 "no improvement"
- 1 "worse"

Robinson PP. Outcome of LN repair. Br J OMS 2000

- 53 pts, 1990-1998, most 3rds
- Delay: 4-47 months (mean=15 months)
- Excised neuroma: 4-14 mm (mean=9.4 mm)
- CD: improved 0 to 51%, PP: improved 34 to 77% (43%)
- No correlation with delay from injury
- No reduction in pain (dysesthesia)
- No patient became completely normal
- Most patients considered surgery worthwhile

Susarla S, Kaban LB. Does early repair of LN injuries improve FSR? JOMS 65: 1070, 2007

- n=64 LN repairs
- Early (<90 days), late (>90 days)
- Mean repair time: 153 days (5 months) (31-1606)
- 22% had early repair (<90 days)
- 93% of early vs. 63% of late repairs returned to FSR within 1 year (p=.05)

Bagieri, Meyer. Review of 222 LN injuries. JOMS 68: 715, 2010

- 1986-2006 (20 years)
- n=222, 171 women, 51 men
- Mean age: 31.1 years (15-61)
- > 1 year followup
- 90% 3rds, 6% SSO, 5% local anesthetic
- 55% numbness, 42% numbness + pain
- Mean injury to repair: 8.5 months (1.5-96)

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Meyer, 2010

- 69% neurorrhaphy, 13% decompression, 8% nerve graft (gr. auric. or sural)
- Results used the Medical Research Council Scale of neurosensory function
- 90.5%: 146 "complete recovery," 55 "useful sensory function"
- 9.5%: 21 patients "no or inadequate improvement"

Meyer, 2010

- Shorter delay = improved outcome
 - With each month, odds of improvement decreased by 5.8%
 - 9 months is a critical time point
- Increased age = worse outcome
 - 5.5% decrease in chance of recovery for every year over 45
- Pain improved more than numbness

Bagheri SC, Meyer RA. Microsurgical repair of the IAN: Success rate and factors that adversely affect outcome. JOMS 2012.

- n=167 pts by one surgeon, 1986-2005
- At least 1 year fu
- 41 male, 126 female, mean age: 38.7 yrs
- Mean time injury-repair = 10.7 mo (0-72 mo)
- FSR (via MRCS) in 152 (81.7%)
- Linear correlation of repair time and success (11% drop per month), significant drop at 12 mo
- Patient age significant, threshold drop at 51 yrs
- Etiology, operative findings, surgery done-no effect
- Presence of pain not significant in achieving FSR (p=.08)

Trigeminal Nerve Injury, OMS Clinics North America, 1992

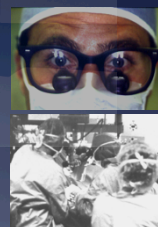
- Multi-site, retrospective study of 521 pts
- 192 IAN hypoesthesia
- 131 LN hypoesthesia
- 124 IAN hyperesthesia
- 74 LN hyperesthesia
- "Success" criteria
 - Light touch detected > 80% of the time
 - Postoperative pain \geq 30% reduction

OMS Clinics NA, 1992 Study

- Overall success = 76.2%
- Hypos (85%) better than hypers (62%)
- Hypo-LN (87%) = Hypo-IAN (85.4%)
- Hyper-LN (67.5%) > hyper-IAN (55.6%)
- Worst results for hyper-IAN (55.6%)
- Decreased success after 6 months

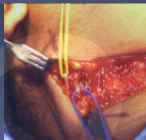
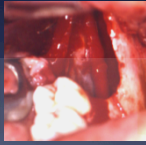
Microneurosurgery

- Magnification (3.5x, 12x)
- Surgical access
- Neurolysis
- Nerve stump preparation
- Neurorrhaphy



Surgical Access

- Transoral
- Transfacial
 - IAN (posterior to 3rd)
 - Need for greater auricular graft
 - Extraoral approach to fracture or bony reconstruction



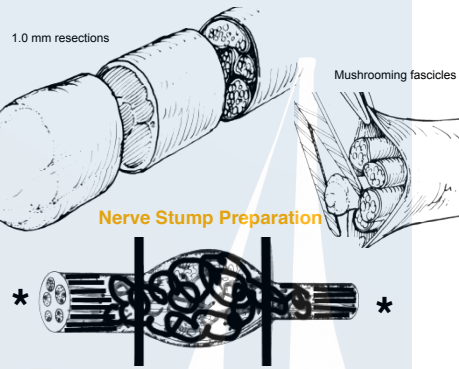
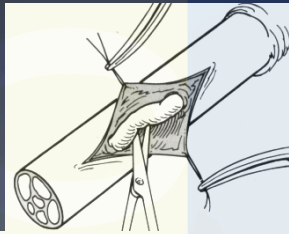
'External' Neurolysis

- Nerve decompression
- Release nerve from surrounding tissues (root, implant, jaw, ZMC fracture)



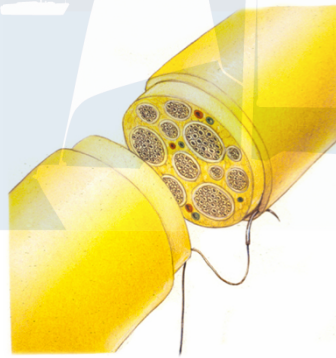
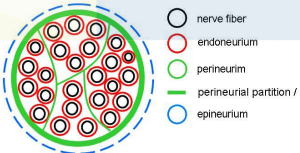
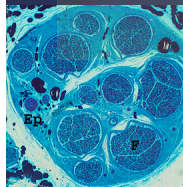
'Internal' Neurolysis

- Not done for polyfascicular nerve

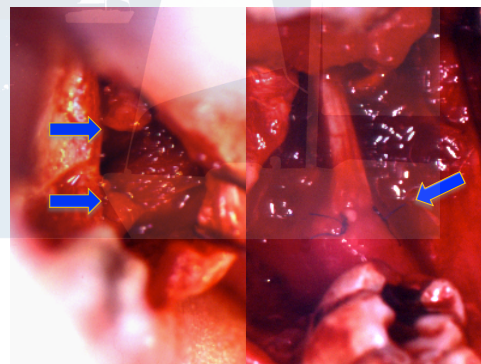
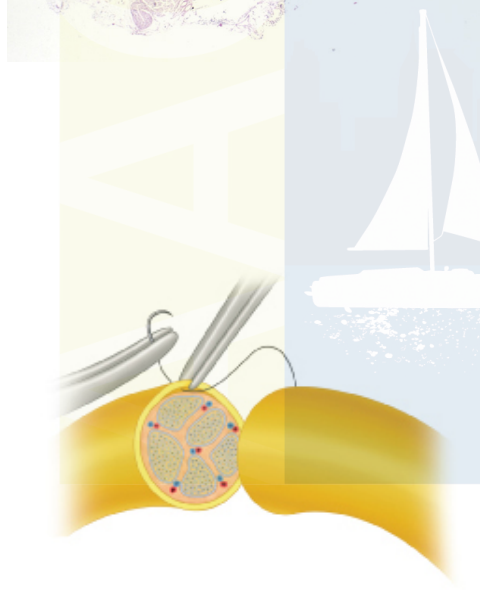
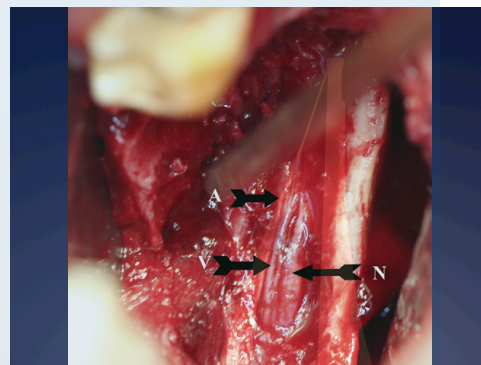
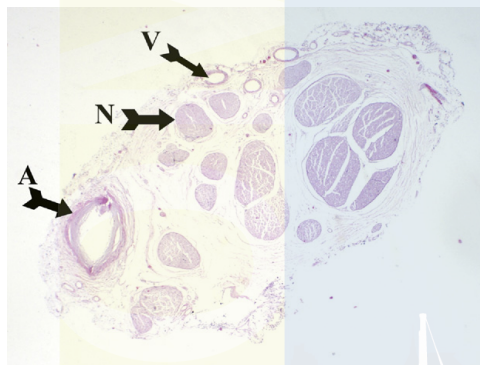
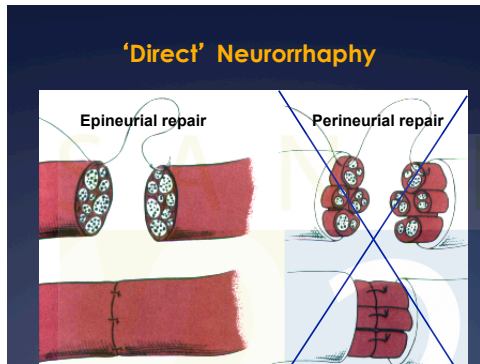


Coaptation

- Align fascicles for direct repair
- Not for polyfascicular nerve



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Scar Reduction at Neuroorrhaphy

- Cyanoacrylate in nerve repair. Int J OMS 39: 705, 2010
- Laser welding (CO₂, argon, Nd-YAG)
- Additives (experimental)
 - Anti-inflammatories, to inhibit of collagen synthesis
 - Corticosteroids (triamcinolone, methylprednisolone)
 - Glycosaminoglycans (OTR4120, ADCON-T/N)
 - Aprotinin, cis-hydroxyproline, human amniotic fluid, hyaluronic acid, tissue plasminogen activator (TPA)
 - Low-dose external beam XRT (700 cGy)
- Ngeow WC. Scar less: Methods of scar reduction at sites of peripheral nerve repair. OOOE 109: 357, 2010

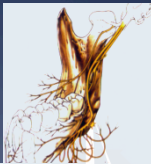
'Indirect' Neuroorrhaphy

- Interpositional nerve graft
 - Autogenous
 - Sural
 - Greater auricular
 - Allogeneic
 - Cadaveric
- Conduit (gap) repair

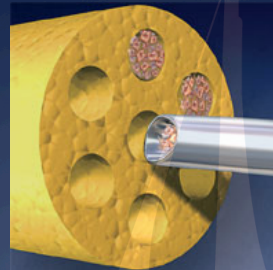


Nerve Graft Indications

- Any significant tension
- IAN gaps > 5-10 mm
- LN gaps > 10-15 mm



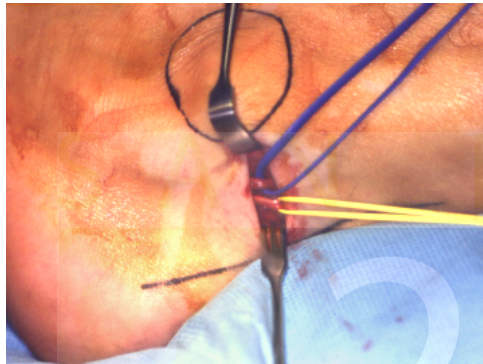
Nerve Grafts = Conduits



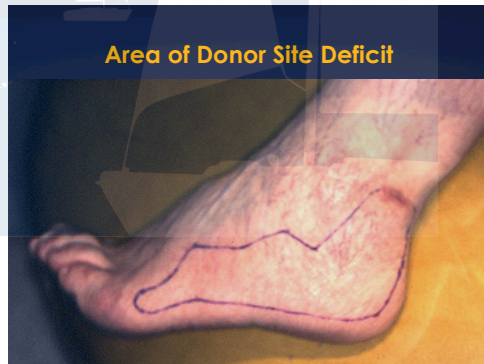
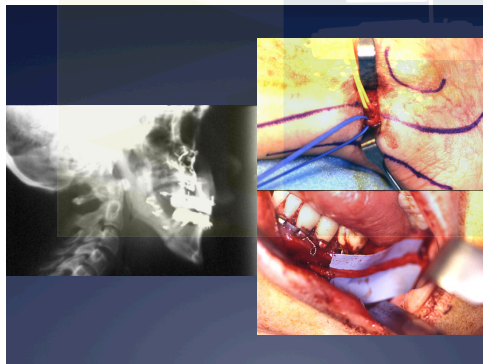
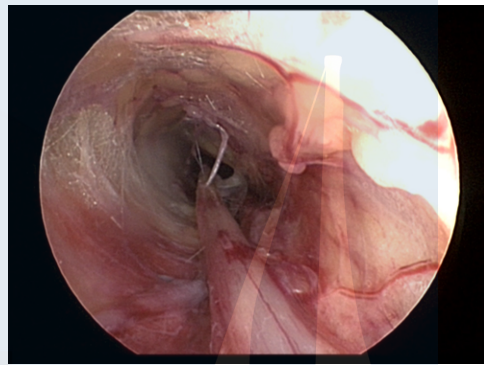
Sural Nerve

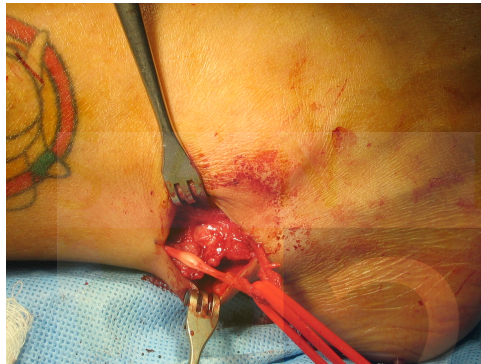
- Medial sural cutaneous nerve
- Sacral plexus S1S2
- Sensory innervation
 - Posterior leg
 - Dorso-lateral foot
- First choice for trigeminal grafts
- Harvest ≥ 20 cm, if necessary
- No repair of sural nerve defect in leg



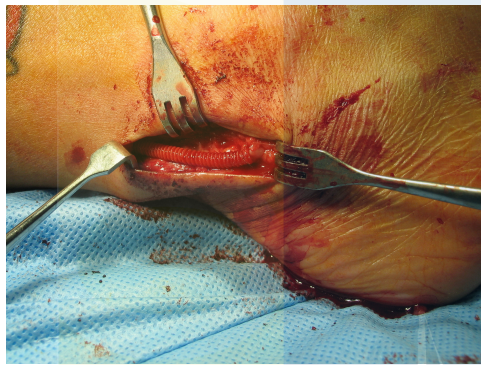


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Miloro M. Subjective outcomes following sural nerve repair. JOMS 63: 1150, 2005

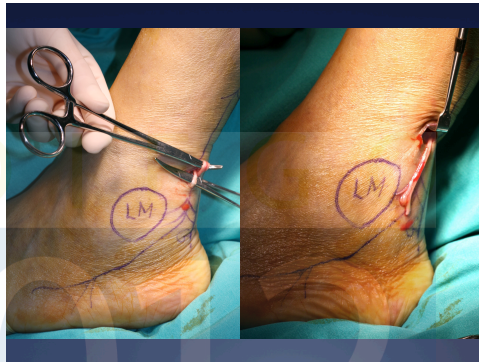
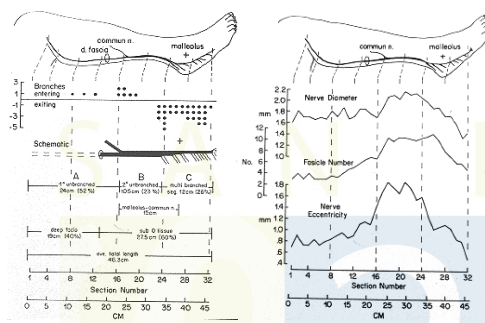
- n = 42 sural grafts
- Follow-up > 20 months
- Questionnaire study
- Compared immed post-surgery to current
- Numbness score (3-10): 5.46 to **1.31**
- Pain score (0-6): 2.15 to **0**
- Cold sensitivity score (0-2): 0.50 to **0**

Miloro M, JOMS 2005

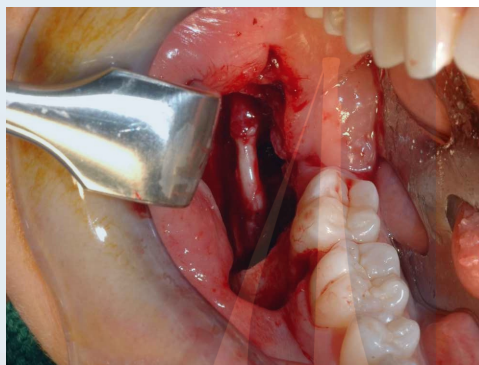
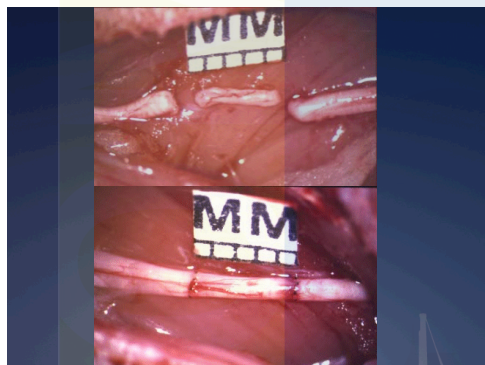
- Final size of deficit area
 - < quarter (1"): **58%**
 - Quarter: **39%**
 - Tennis ball/orange: 4%
 - Softball/grapefruit: 0%
 - Larger: 0%
- Positive correlation between trigeminal and sural recovery



| | Sural (2.1 mm) | Gr. Auric (1.5 mm) |
|--------------|----------------|--------------------|
| IAN (2.4 mm) | 87% | 63% |
| LN (2.6 mm) | 83% | 59% |

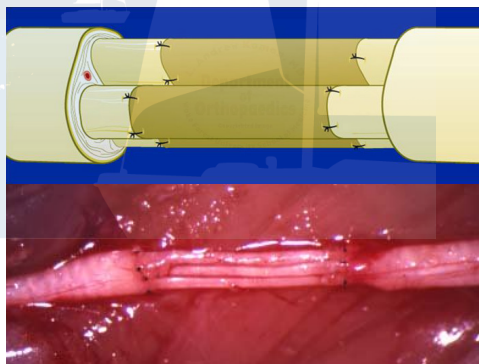


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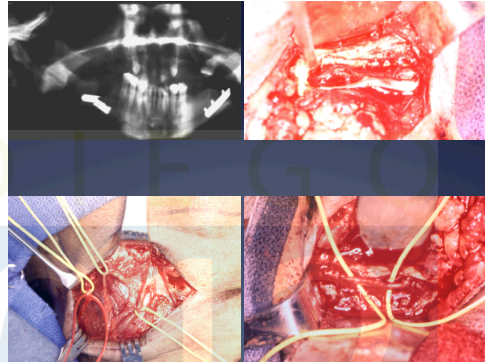
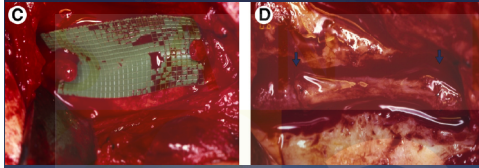


Greater Auricular Nerve

- Cervical plexus C2C3
- Poor choice
 - Small diameter
 - Facial scar
 - Sensory deficit on face
 - Inferior ear, angle of jaw
- Indications
 - Same surgical site
 - Cable graft
 - Nerve transfer

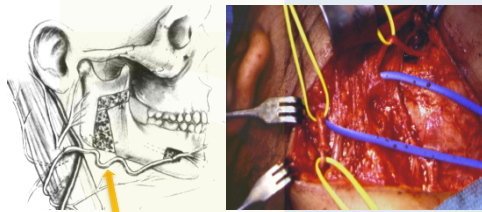


IAN Repair with Greater Auricular Nerve Graft



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Nerve Transfer



Greater Auricular--Sural--Mental

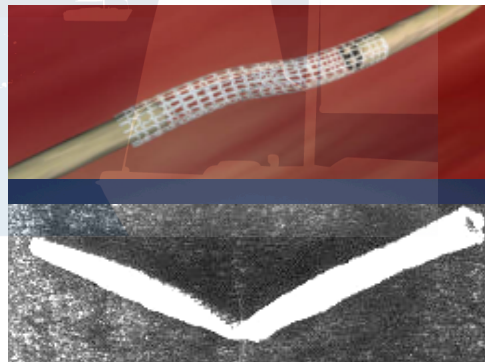
Conduit Repair

- Gap repair
- Entubulation repair




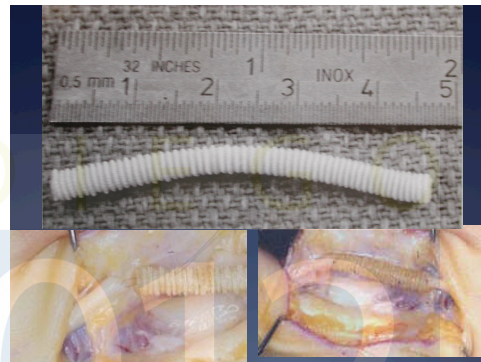
Conduits: Alloplastic

- Polyglycolic acid
- Polyester
- Gore-tex (e-PTFE)
- Silastic tube

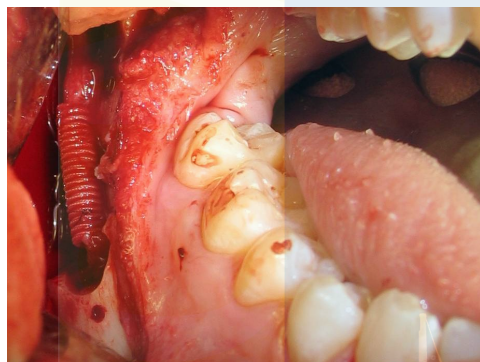


Neurotube®

- Bioabsorbable nerve conduit
- Polyglycolic acid (PGA)
- Porous
- Flexible
- Corrugated
- 2.3 mm diameter
- 4 cm length
- www.neurotube.com

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Nerve Connector/Protector

- 3D extracellular matrix
- Resorbable
- Conduit repair
- Protection of anastomosis site






This price list contains the AxoGen, Inc. product line for the AxoGuard® Nerve Protector and AxoGuard® Nerve Connector. Product packages contain one AxoGuard® Nerve Protector or Nerve Connector.

TO PLACE AN ORDER: Contact your local distributor for an order through AxoGen Customer Service. PHONE: 800-452-3333 (1-800-452-3333) FAX: 314-332-8251 Email: customerservice@axogen.com

| Product Code | Size (dia. x length) | Material | Unit Price |
|--------------|----------------------|------------|------------|
| AG0000 | 3.0mm x 30mm | Collagen | \$1300 |
| AG0001 | 3.0mm x 30mm | Muscle | \$1300 |
| AG0002 | 3.0mm x 30mm | Fascia | \$1300 |
| AG0003 | 3.0mm x 30mm | Vein graft | \$1300 |
| AG0004 | 3.0mm x 40mm | Collagen | \$1450 |
| AG0005 | 3.0mm x 40mm | Muscle | \$1450 |
| AG0006 | 3.0mm x 40mm | Fascia | \$1450 |
| AG0007 | 3.0mm x 40mm | Vein graft | \$1450 |




AXOGUARD®
Nerve Protector and Nerve Connector


AXOGUARD®
Nerve Connector

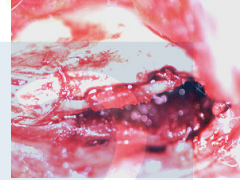
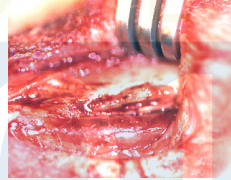
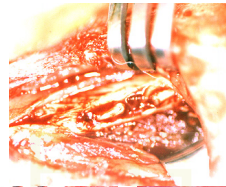
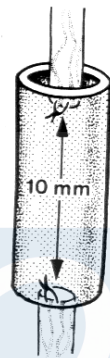
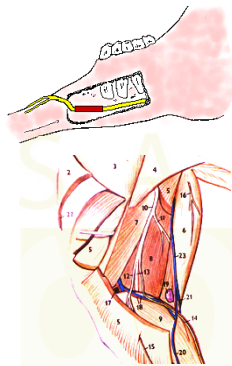
AXOGEN, INC.
31400 Perimeter Blvd., Suite 100
Atlanta, Georgia 30328
Phone: 800-452-3333
Fax: 314-332-8251
www.axogen.com

Manufactured by:
Collagen: Collagen Corporation
Muscle: National Muscle
Fascia: National Muscle
Vein Graft: National Muscle

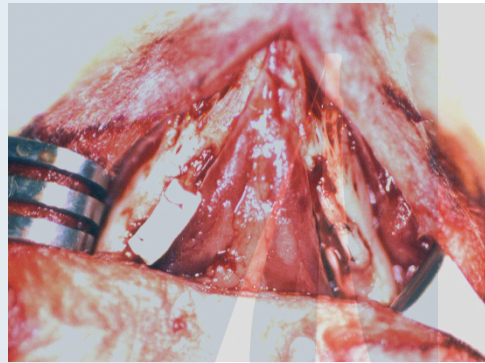
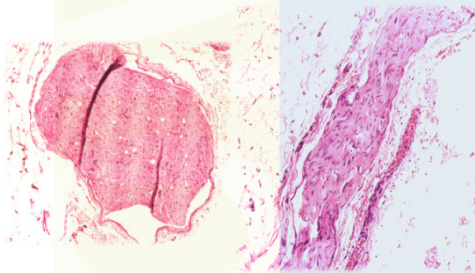
Conduits: Autogenous

- Collagen
- Muscle
- Fascia
- Dura mater
 - No longer used
 - Jacob-Creutzfeldt disease, MMWR 1996
- Vein
 - Abundant, no morbidity
 - NGF on endothelial, advential surfaces





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Gore-tex conduit **Tibial nerve graft**

Cadaveric Nerve Graft (Axogen)

- Decellularized allogeneic graft
- Green J. Use of decellularized human nerve grafts for IAN and LN. JOMS Suppl 2009
- 8 pts (5LN, 3 IAN)
- 4 pts, some recovery (50% 'success')
- **1 pt, minimal recovery**
- **3 pts, no recovery**



Nerve Graft
Repairing nerves with nerves.

AVANCE Nerve Graft, a human allograft nerve, is for the repair, replacement and reconstruction of damaged peripheral nerves. It is initially processed to preserve the three dimensional structure of the nerve and the inherent growth properties that it offers. This process cleans the cellular and non-cellular material from the tissue, while cellular debris, axons as well as dystrophic axolemma (myelin sheath) are gradually occurring (reducing) to axon regeneration. The resulting nerve graft provides a sterile scaffold that allows the natural healing process to repair peripheral nerves.

AVANCE Nerve Graft is placed into the nerve defect to fill the gap. It is supplied sterile in a variety of lengths and diameters.

AVANCE Nerve Graft is implanted using microsurgical techniques, similar to autograft.



Only Distributed Allograft Nerve

- REGULATED GRAFT
- FREE DISEASED TISSUE (DEBRIDED)
- FREE DISEASED NERVE (STRIPPED)
- GRAFTS STORED IN A STERILE MEDIUM

Repairing Nerves with Nerve

- MAINTAINS NERVE'S INHERENT GROWTH PROPERTIES
- FREE DISEASED TISSUE (DEBRIDED)
- GRAFTS STORED IN A STERILE MEDIUM
- GRAFTS STORED IN A STERILE MEDIUM

| Actual sizes may vary | PRODUCT CODE | SIZE | DIAMETER | LENGTH |
|-----------------------|--------------|------|----------|--------|
| | 111215 | 1 | 1-2 mm | 15 mm |
| | 211215 | 2 | 2-3 mm | 15 mm |
| | 111230 | 1 | 1-2 mm | 30 mm |
| | 211230 | 2 | 2-3 mm | 30 mm |
| | 311230 | 3 | 3-4 mm | 30 mm |
| | 411230 | 4 | 4-5 mm | 30 mm |
| | 111250 | 1 | 1-2 mm | 50 mm |
| | 211250 | 2 | 2-3 mm | 50 mm |
| | 311250 | 3 | 3-4 mm | 50 mm |
| | 411250 | 4 | 4-5 mm | 50 mm |

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| Avance® Nerve Graft | | | |
|---------------------|--------|--------------|------------|
| Diameter | Length | Product code | Cost (USD) |
| 1-2 mm | 15 mm | 111215 | 1150 |
| 2-3 mm | 15 mm | 211215 | 1150 |
| 3-4 mm | 15 mm | 311215 | 1150 |
| 4-5 mm | 15 mm | 411215 | 1150 |
| 1-2 mm | 30 mm | 111230 | 1750 |
| 2-3 mm | 30 mm | 211230 | 1750 |
| 3-4 mm | 30 mm | 311230 | 1750 |
| 4-5 mm | 30 mm | 411230 | 1750 |
| 1-2 mm | 50 mm | 111250 | 2150 |
| 2-3 mm | 50 mm | 211250 | 2150 |
| 3-4 mm | 50 mm | 311250 | 2150 |
| 4-5 mm | 50 mm | 411250 | 2150 |

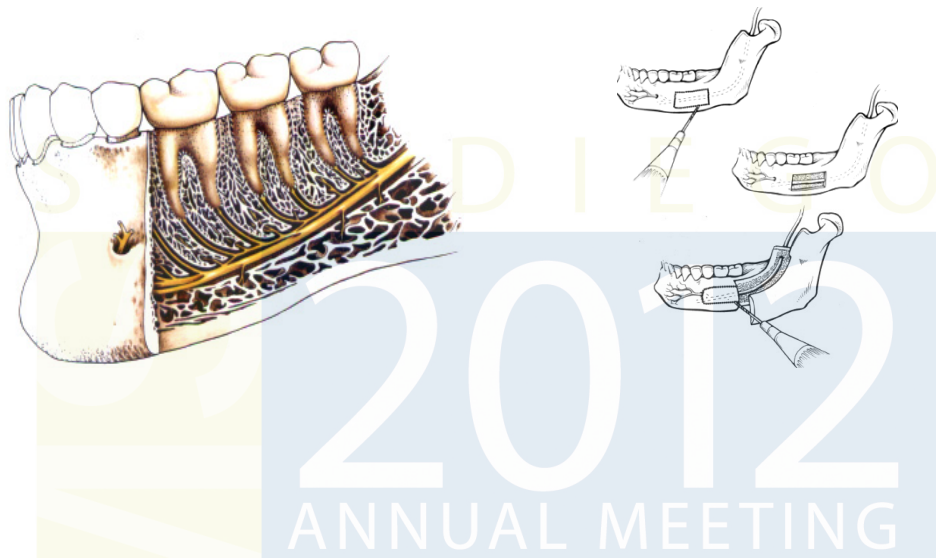
Nerve Redirection Procedures

- A. Excise painful neuroma and 'bury' into muscle or bone
- B. Suture mental nerve into orbicularis oris for collateral axonal sprouting

Neurosensory Recovery

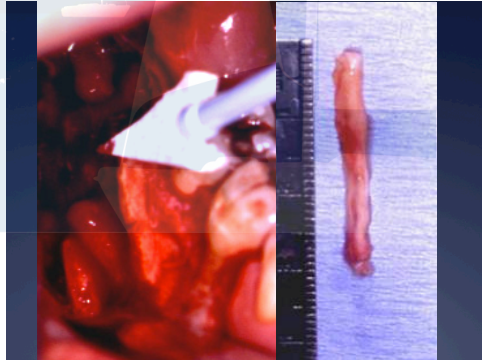
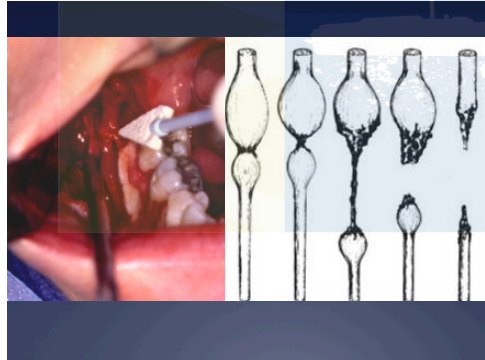
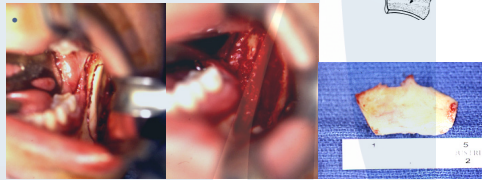
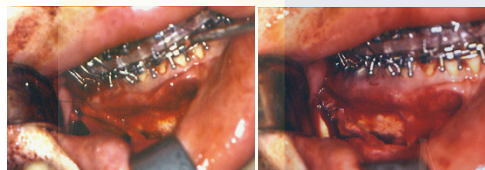
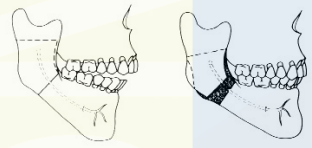
- Nerve regeneration
 - 1 mm/day
 - 1 inch/month
 - From cell body (ganglion) to lip or tongue
- Direct repair
 - Ganglion to lip=10 cm (100 days)
- Slower thru nerve graft repair (3-6 months)

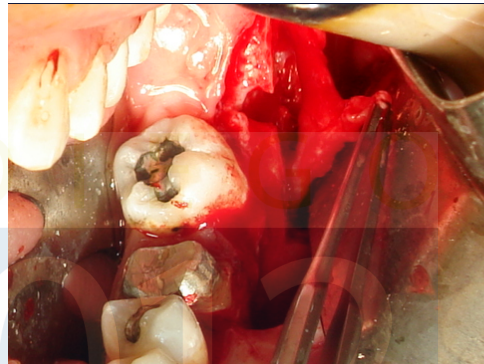
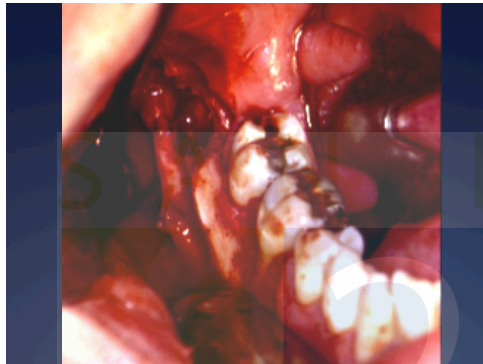
Sensory Re-education Exercises 'Biofeedback'



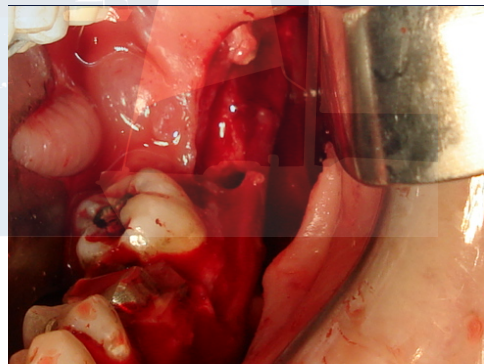
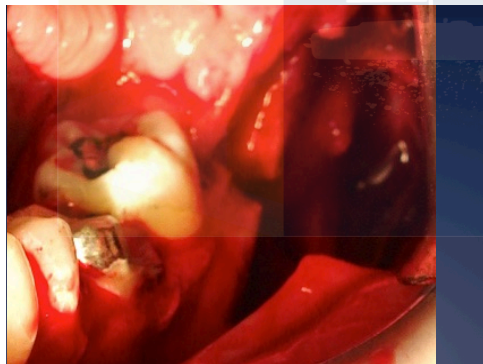
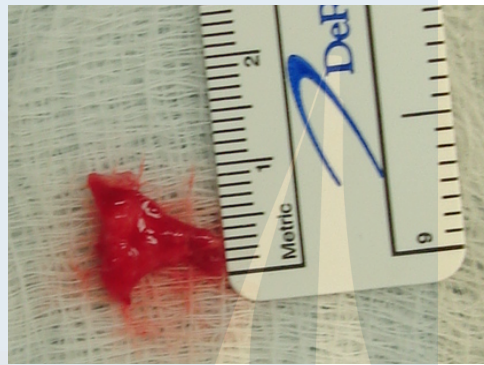
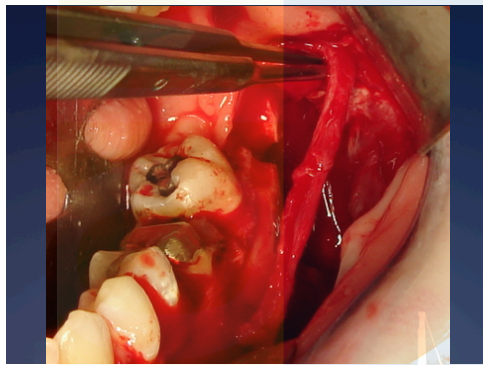
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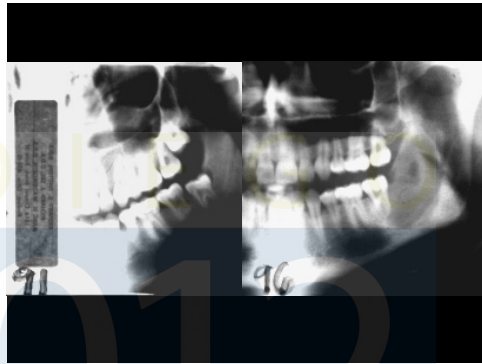
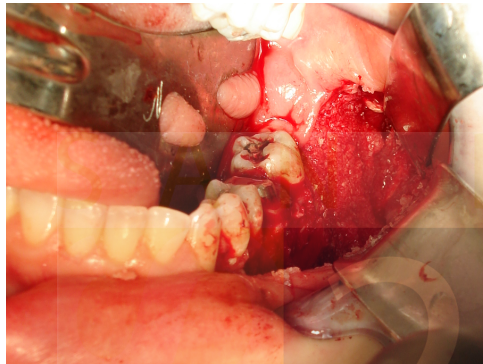
Miloro M. Surgical access for inferior alveolar nerve repair. JOMS 53: 1224, 1995



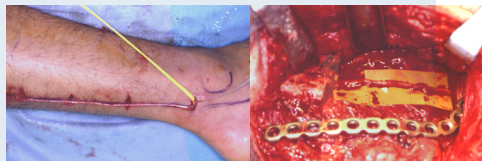
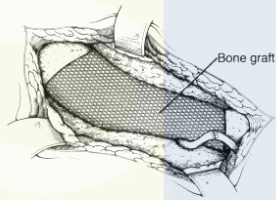
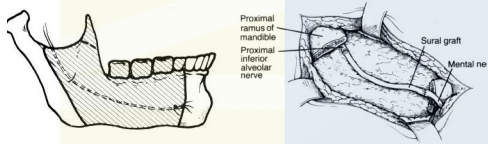


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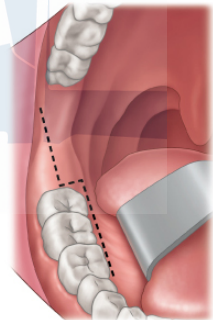
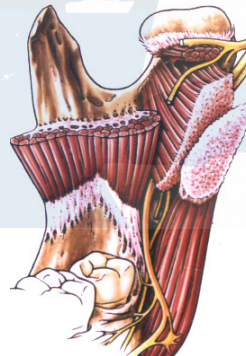
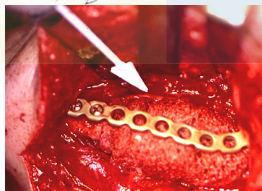
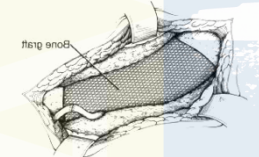


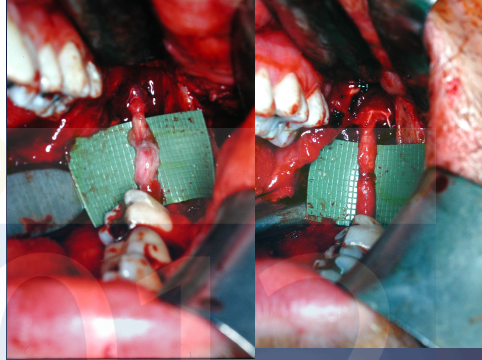
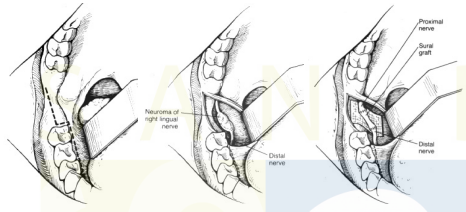


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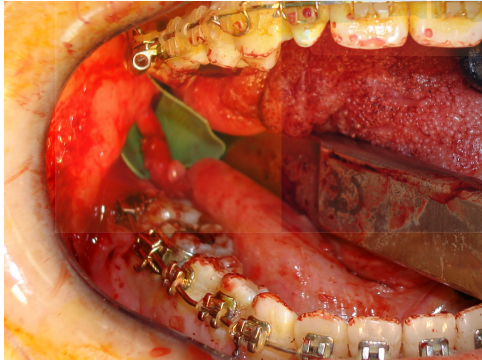
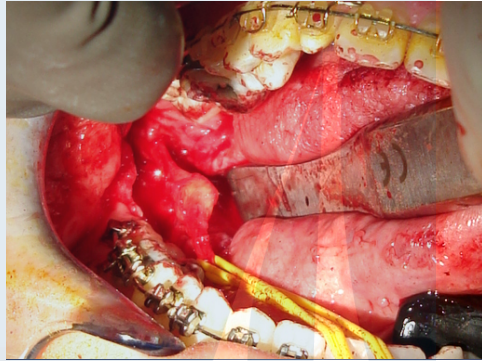
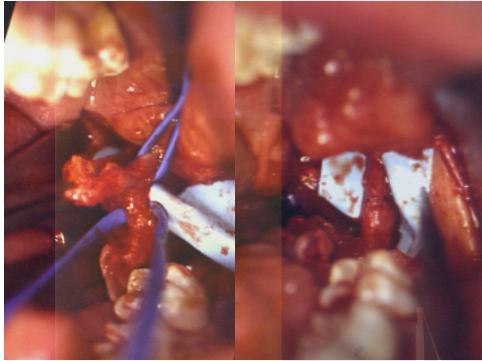


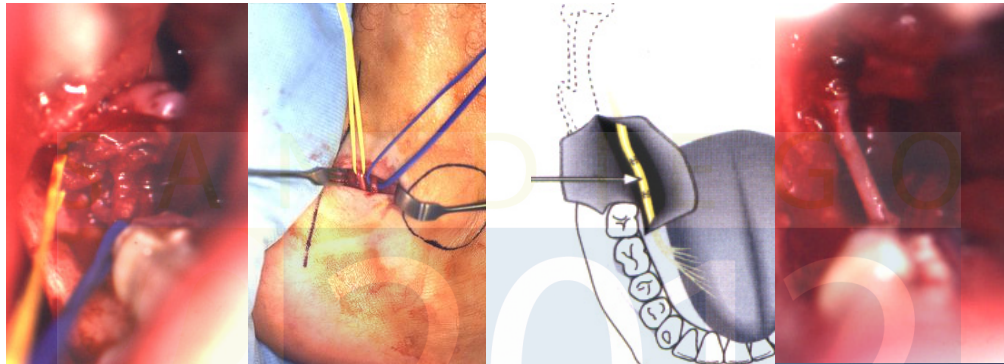
Miloro M, Halkias LE. Bone graft stabilization using knitted dexon mesh. JOMS 55: 1026, 1997





2012
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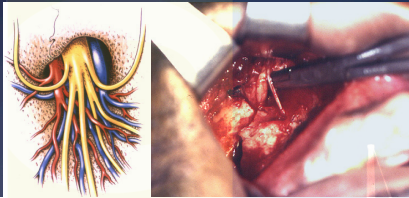




2012
ANNUAL MEETING

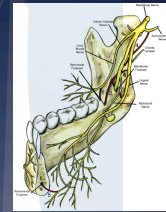
Infraorbital Nerve Repair

- Multiple small (0.5-1.0 mm) branches
- Rarely transected, or in need of repair



Long Buccal Nerve

- Small nerve diameter (0.5-1.0 mm)
- Commonly injured
- Minimal sensory deficit
- Uncommonly repaired



Patient Scenarios

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Patient One

- 21 year old man
- 3rds 6 months ago
- 'Decreased sensation lip/chin'
- VAS = 2/10
- CNT = Sunderland IV (~10%)

Patient Two

- 45 year old woman
- Implant #19 6 months ago
- Not in canal on radiograph
- Developing hypersensitivity LLC
- VAS = 9/10 with pain
- CNT = Sunderland I (100%)

Patient Three

- 39 year old man
- Occlusal amalgam #30 2 months ago
- Numbness, pain of R lower lip, not chin
- VAS = 4/10
- CNT = Sunderland IV focal at vermillion
- CNT = Sunderland I most of LLC

Patient Four

- 27 year old woman
- 3rds removed 8 months ago
- Immediate anesthesia, improved for 1st 3 months only, now left with 'decreased feeling LLC'
- VAS = 6/10
- CNT = Sunderland II (85%)

Patient Five

- 31 year old woman
- 3rds removed 3 weeks ago
- Hypersensitive LLC to lipstick
- VAS = 10/10
- CNT = Sunderland I (100%)

