Botulinum Neurotoxin Chemodenervation Procedures: Limb Spasticity and Dystonia

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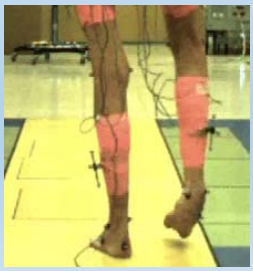
Chemodenervation Procedures for Limb Spasticity and Dystonia:

Agenda

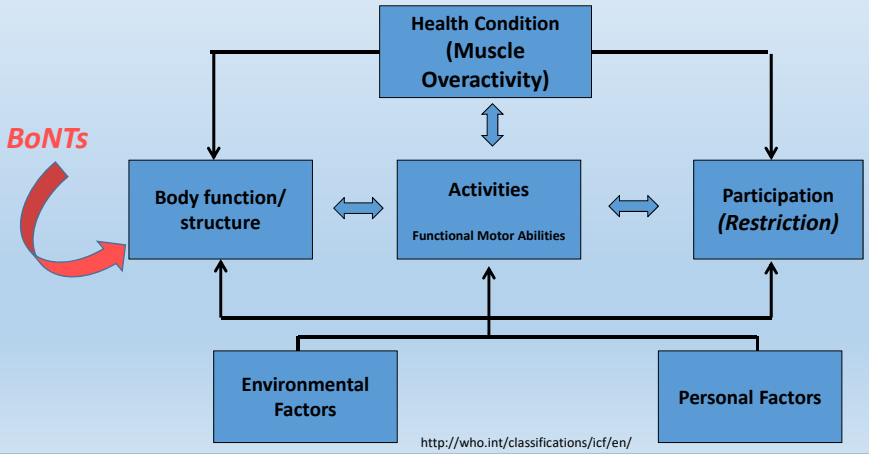
- Which conditions?
- Who needs treatment and why?
  - Patient assessment
  - Setting Goals
  - Muscle selection
- Which treatment option?
  - Selecting the optimal procedure
  - Toxin dosing
- Optimizing procedure outcome
  - Guidance/localization
  - Post procedure care
- Putting it all together: Case studies

Spasticity, lumbricals:
MCP joint flexion,
IP joint extension



Focal lower limb dystonia:
True equinus

International Classification of Functioning, Disability, and Health



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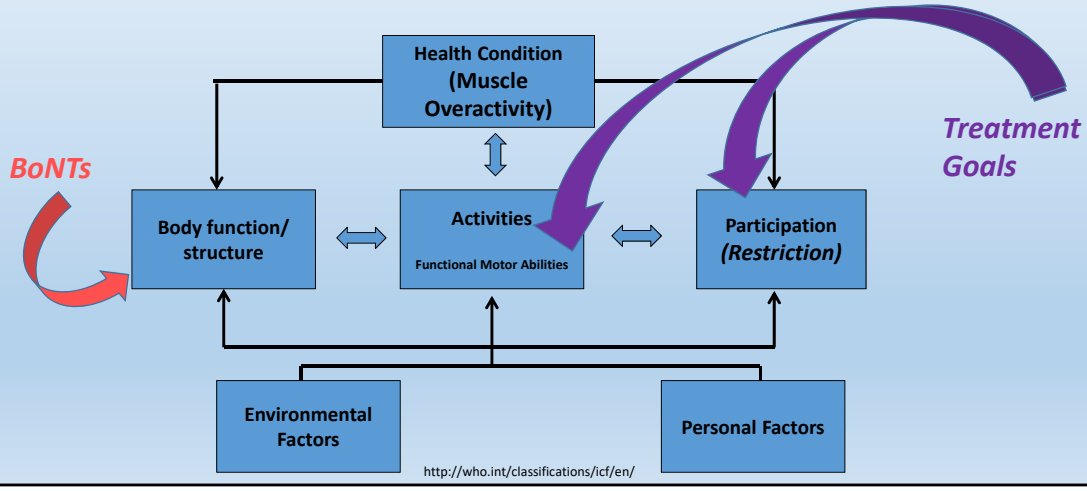
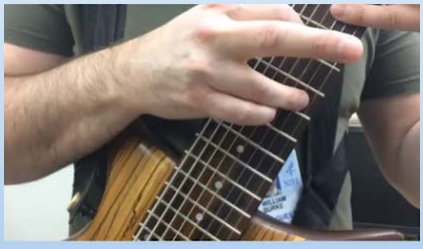


BoNT/Chemodenervation for Treatment of Limb Spasticity and Dystonia: Caveats

- Only problematic spasticity or dystonia require treatment
- Problems may include
  - Passive function
    - ADLs, transfers, skin integrity, positioning
  - Active function
    - ADLs, Mobility, other
  - Quality of life
    - Sleep
    - Pain

BoNT/ for Treatment of Limb Spasticity and Dystonia: Caveats

- BoNT: first line treatment for focal, multifocal or segmental dystonia or spasticity



BoNT for Treatment of Limb Spasticity and Dystonia: Caveats

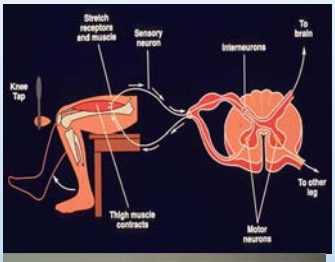
- BoNT for generalized spasticity or dystonia:
  - A limited number of muscles can be treated at one session
    - Minimum effective dosage/muscle
    - Maximum total dosage/session
- BoNT may be useful
  - To treat a focal problem
  - As an adjunct to other treatment
    - Oral medications
    - Other chemodenervation agents
    - Surgery: DBS, ITB, SDR

BoNT/Chemodenervation, Which Conditions?

Limb Spasticity and Dystonia

UMNS Related Spasticity: *Motor Disorder Characterized by*

- **Spasticity**
  - Is a motor disorder characterized by
  - Velocity-dependent increase in tonic stretch reflexes (muscle tone)
    - Exaggerated tendon jerks
  - Results from hyperexcitability of the stretch reflex
  - **One component of the upper motoneuron syndrome**



Lance, 1980, Ivanhoe CB, Reistetter TA. *Am J Phys Med Rehabil.* 2004;83(Suppl):S3–S9. Simpson DM et al. *Neurology.* 2008;70:1691–1698. Satkunam LE. *CMAJ.* 2003;169(11):1173–1179. Ward AB. *J Neural Transm.* 2008;115:607–616.

UMNS Related Motor Disorders and Function

Negative

Weakness

Poor selective motor control

Sensory deficits

Balance and coordination problems

UMNS
Stroke
Acquired Brain Injury
Cerebral Palsy
Spinal Cord Injury
MS
Others

MSK Consequences:
Contractures, torsion, dislocation

Positive

Abnormal reflexes

Hypertonia
- **Spasticity**
- **Dystonia**

Involuntary movements

BoNTs

Function

UMNS Motor Impairments: Who Needs Treatment?

Cerebra Palsy, Diplegia:
Spasticity limiting gait

Cerebral Palsy, Quadriplegia:
Hypotonia/weakness: limiting gait

Classification of Spasticity: Distribution and Severity

- **Generalized/**diffuse, but may
  - Be asymmetric
  - Affect upper or lower limbs differently
- **Regional/multi-limb**
  - E.g., spastic diplegia
- **Multifocal**
  - E.g., several joints affected in the same limb
- **Focal**
  - **Striatal toe**, flexed elbow, adducted thigh
  - ***Caveat:*** *Spasticity may be generalized but cause a focal functional problem amenable to local treatment*
- **Severity:**
  - Mild, moderate, severe

Ward AB. *J Neural Transm.* 2008;115:607–616. Brin MF et al. *Muscle Nerve*. 1997;20(suppl 6):S208-S220.

Chemodenervation, which Conditions?

Limb Dystonia

Dystonia

- Motor disorder characterized by postures which may be
  - Sustained or intermittent
  - Often have a twisting characteristic
  - May be tremulous
  - May be fixed or hyperkinetic

Hemidystonia

Generalized Dystonia

Dystonia: May be Associated with

- **Movements/postures can be**
  - Hyperkinetic
  - Fixed
- **Muscle tone:**
  - Normal
  - Hypotonic
  - Hypertonic

Fixed postures :Dystonia

Hyperkinetic Dystonia

Dystonia: May be Associated with

- Tone:
  - Normal tone
  - Hypotonia
  - Hypertonia
- Postures
  - Hyperkinetic
  - Fixed
- **Mirror dystonia**
- **Overflow movements**
- **Tremor**

Post Stroke Dystonia -Mirror Dystonia

Post Stroke Dystonic Tremor

Spectrum of Limb Dystonia

- **Dystonic postures/movements**
  - Typically triggered by movement or attempted movement
    - Even by attempts to relax
  - **Impairs motor coordination including**
    - Timing, speed, excursion, directionality, smoothness, effort
- **Presentation** Is variable: postures differ between patients
- **May Involve any muscle or groups of muscles**
- **Postures/Involvement** in a specific patient are typically repetitive/similar
- **Postures** may have
  - A wide ranging impact on function, quality of life
  - Unpredictable/adverse effect on interventions targeting other impairments

Spectrum of Dystonia: Generalized Dystonia

Spectrum of Dystonia: Adult Focal Limb Dystonia:

- Examples
  - Lower limb runner's Dystonia with foot inversion
  - Upper limb, focal hand dystonia
    - Writer's or musician's cramp
    - Others
- May be associated with sensory tricks or geste

62 y.o. with "runner's dystonia"

50 y.o. with focal hand dystonia/Geste

Focal Limb Dystonia:

- Task Specificity
  - **Upper limb:** typically remains task specific
  - **Lower limb:** Task specific at onset but may generalize
- Task specificity should be assessed in all patients with focal dystonia
  - Upper limb: writing, typing, playing musical instrument
  - Lower limb: walking, running, marching, backwards walking

Which Patient's Need Treatment?

Patient assessment identifies if Spasticity or Dystonia Requires Treatment

Patient Evaluation and Treatment Planning

- Treatment is only required for problematic spasticity and dystonia, assessed by
- History:
  - Onset, progression, diurnal variation, factors that provoke or improve MoA
  - Comorbidities
- Impairment Assessment
  - Neurological exam
    - Tone, reflexes, motor control weakness
    - Involuntary movements/postures
    - Severity/scope of the problem
  - Musculoskeletal exam
    - Contractures or ROM limitations?
- Functional Assessment

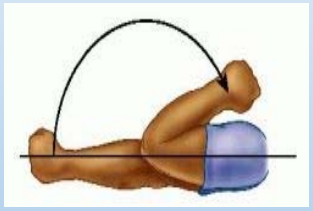
CP, diplegia, Spasticity

Dystonia, Involuntary Movements/Overflow with talking

Impairment Assessment: Spasticity Scales: Modified Ashworth Scale (MAS)

MAS	mMAS	Description
0	0	No increase in muscle tone
1	1	Slight increase in muscle tone, manifested by a catch and release
1+	2	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance
2	3	More marked increase in muscle tone, but affected part (s) can easily be moved
3	4	Considerable increase in muscle tone, passive movement difficult
4	5	Affected part (s) rigid in flexion or extension

MAS=Modified Ashworth Scale, mMAS=Modified-Modified Ashworth Scale



- ***MAS: the most widely used "spasticity" assessment scales***

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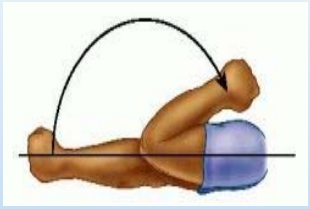


- ***Does the MAS assess spasticity as defined by Lance?***
  - *Performed at one speed*
    - ***Speed of the limb falling with gravity (1 second)***
    - ***Not performed at a rapid speed***
  - ***Resistance is influenced by***
    - *Any increased tone: spasticity, rigidity, hypertonic dystonia with co-contraction*
    - *Non-contractile elements of muscle*
  - ***Therefore the MAS is more a measure of stiffness or resistance to ROM than spasticity***

Balci BP, Noro Psikiyatr Ars. 2018

Impairment Assessment, Beyond the MAS: Tardieu or Modified Tardieu Scale (MTS)

- Advantage 1
  - Assesses muscle tone at 2 speeds
    - Slowly (V1 or R2)
    - As Fast as possible (V2 or R1)
      - Measures velocity dependent tone
- Measure
  - **Slow speed/V1 or R2**:
    - Assesses the extent of **PROM**
  - **Fast spee/V2 or R1:**
    - Assesses **velocity dependent** muscle tone

Gracies JM et al Arch Phys Med Rehabil 2010

MTS: Knee extensors & flexors

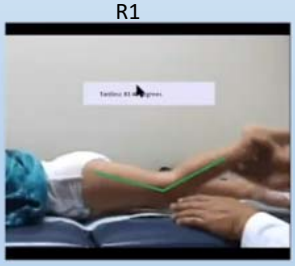
Spasticity Scales: Tardieu Scale

- Advantage 2
  - Quantitative, not ordinal measure of spasticity
    - A "Spasticity or catch angle" is calculated
      - R2(V1)- R1(V2) = Spasticity angle
  - **Large angle or** difference = greater contribution of dynamic spasticity
  - **Small angle or** difference = limited ROM more than dynamic tone issue
    - Indicates some level of contracture

Gracies JM et al Arch Phys Med Rehabil 2010

R2

R1



Spasticity Angle = V1 or R2 (150°) – V2 or R1 (40°) = 110°

Hypertonia Assessment Tool

- Discriminative Scale
  - **Spasticity**
  - Dystonia
  - Rigidity
- Evaluates
  - **Velocity dependent increased tone**
  - **Abnormal postures, co-contraction**
  - **Biphasic tone**

Marsico P, J Child Neurol 2017, Mink JA et al Dev Med Child Neurol. 2010

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    - **Movement of distant body part**
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Hypertonia Assessment Tool

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Marsico P, J Child Neurol 2017, Mink JA et al Dev Med Child Neurol. 2010

Spasticity and Dystonia: Caveats

- Spasticity:
  - It is appreciated or **"felt"** by the examiner on
    - During physical exam
- Dystonia
  - Is most often appreciated or **"seen"**
    - When a patient initiates movement
    - Attempts to move
    - Or attempts to relax
    - Or when performing non-movement tasks like talking

CP, diplegia, Spasticity

Dystonia, Involuntary Movements/Overflow with talking

Beyond Impairment: Assessing Function

- **Assessment of function/movement should detail**
  - Pattern, scope, severity
  - At rest/with activities
  - Impact on function
- **How?**
  - Observation
  - Observation + video
  - Motion analysis
- **Assess various conditions or tasks**
  - Upper limb: Reaching, grasping, playing instrument etc.
  - Lower limb: Walking, running backwards walking, marching
  - Provoking/non-provoking tasks
- **Assessment provides information about:**
  - Muscle involvement
    - Informing treatment planning/goals
  - Response to treatment
  - Change in pattern over time

Hemidystonia: Pre/Post BoNT Chemodenervation

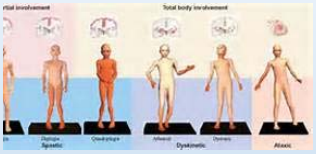
When do we Treat?

Is Spasticity or Dystonia Causing Problems?

What are the treatment goals?

BoNT for MOA, To Treat or Not to Treat, That is the Question……Determined by

- Identifiable Treatment Goals
  - Quality of life: sleep, pain relief
  - Passive function
  - Active function
- Access to care/follow up
  - Compliance
  - Commitment to post intervention care



Setting Goals for BoNT Treatment for Spasticity or Dystoni

- Goals must be **patient focused**
  - **Clearly communicated** to the patient
  - Consider Goal Attainment Scaling (GAS)
- Goals may include
  - Improved active function
  - Improved passive function
  - Comfort: less pain, better sleep, splint tolerance
  - Reduced disfigurement
  - Reduced burden of care

Pre/post BoNT for UL PSS, 7 years post stroke

Jankovic, J, Esquenazi, A, Fehlings, D, et al. *Clin Neuropharmacol.* 2004;27:234-244.

Setting Treatment Goals

- Goals should be **SMART**
  - **S**pecific:
    - Ex: decreased fisting to improve skin hygiene, pain
  - **M**easurable:
    - Ex: measurable improvement in ROM, skin breakdowns
  - **A**chievable/Attainable:
    - Patient has access to therapy etc.
  - **R**elevant/realistic
    - For the patient/family/situation
  - **T**imely:
    - Can be achieved within the proposed time frame

What?

Are the treatment options?

Chemodenervation Options

	Local Anesthetics*	Phenol and Alcohol	Botulinum Toxins Type A & B
Mechanism of Action	Blocks sodium channels/action potential	Protein denaturation/axonal necrosis	Presynaptic inhibition of acetylcholine release
Duration	1-4 hours	20 days-7-18 months	3-7 months
Side Effects	Injection site pain , Temporary weakness, paralysis, sensory loss	Pain, skin necrosis, paresthesias	Injection site pain, weakness, atrophy
When?	Temporary Block	Long term effect	Long term effect

* Lidocaine, Bupivacaine, Etidocaine

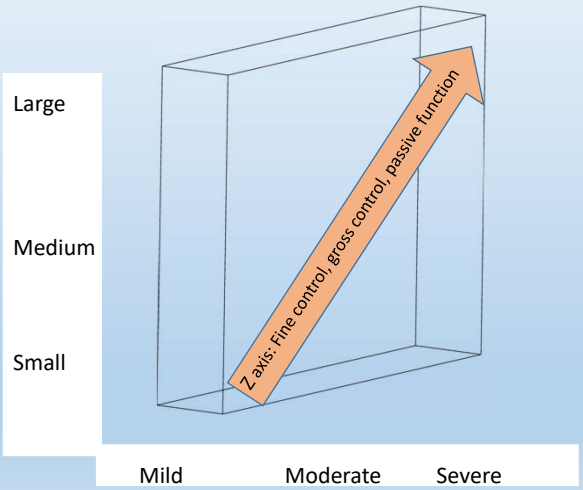
- Carpenter EB, et al. *Dev Med Child Neurol.* 1980.
- Chua KSG, et al. *Arch Phys Med Rehabil.* 2000.
- Kirazli Y, et al. *Am J Phys Med Rehabil.* 1998.
- Kong KH, et al. *Arch Phys Med Rehabil.* 1999.
- Koman LA, et al. *Pediatrics.* 2001.
- Koman LA, et al. *J Ped Orthopaed.* 1994.
- Koman LA, et al. *J Ped Orthopaed.* 1993.
- Love SC, et al. *Eur J Neurol.* 2001.
- Fehlings D, et al. *J Pediatr.* 2000.
- Koman LA et al, *J Ped Orthopaed.* 2000.

Combining Chemodenervation Agents: BoNT + Neurolytics, Why?

- BoNT and neuolytics each have dose limitations
- Combining BoNT and neuroulytics allows greater number of muscles to be treated
- Approach
  - BoNT for smaller distal muscles; smaller dose or when less “permanent effect” is desired
  - Phenol/ETOH for large proximal muscles innervated by easy-to-access motor nerves and motor points

Limb Spasticity and Dystonia: BoNT Dose Calculation Basics

- Dose information is available from
  - Manufacturers
  - Published studies, injection guides
- Rather than using a fixed dose per muscle
- Consider dose calculation in 3 dimensions based on
  - Muscle size
  - Severity of the problem
  - Functional goal

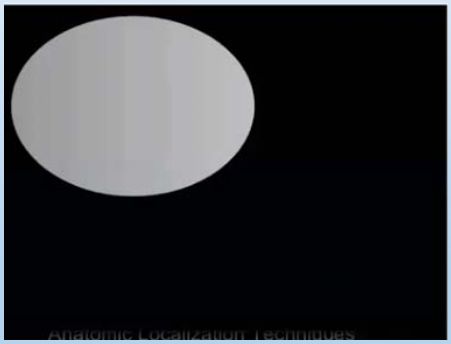


Optimizing Treatment

Improving the accuracy of muscle targeting

Should You Rely Only on Anatomic/Manual Guidance for Chemodenervation Procedures?

- **Knowledge of surface/functional anatomy is essential**
  - Recognizing muscle contributions to abnormal movements/postures
  - Prerequisite for
    - Any invasive procedure including BoNT/phenol/nerve blocks etc.
    - Any use of supplemental guidance
- **Limitations to relying solely on anatomic guidance**
  - Knowledge of anatomy
  - Reference guides not specific for chemodenervation
    - Cannot position the patient as described in atlas
    - Patient cooperation, involuntary movements
    - Anatomic rearrangements/contracture
  - Cannot asses depth of target or muscle thickness



Alter KE, Karp BI, Toxins 2017, Finlayson H et al Clin Rehabil 2016, Grigorui AI et al, Arch Phys Med Rehabil 2015

Chemodenervation Procedures: Why Use a Supplemental Localization or Guidance Technique?

- Comparative studies indicate that
  - **Instrumented guidance is superior to anatomic guidance alone**
    - US and or EMG are superior guiding injections for cervical dystonia
    - US or ESTIM guidance is more accurate than EMG for spasticity indications
    - US is the most anatomically accurate method of guidance
- Injections in the region of the innervation zone/endplate are more effective than injections outside these regions

Ko YD et al 2020 Ann Rehabil, Alter KE, Karp BI, Toxins 2017, Chan, Finlayson et al 2017 Clin Rehabil, Grigoriu AI et al 2015 Archive PMR, H et al, Van Campenhout A, Dev Med Child Neurol 2011

Guidance for BoNT Injections: EMG, E-Stim

Advantages

- Clinician familiarity
- EMG: provides info on muscle activity
- ESTIM: muscle twitch or joint movement may confirm needle location

Disadvantages/Limitations

- EMG ESTIM cannot
  - Estimate target depth, anatomic variation or rearrangement, safe path to target
  - Position patients per print reference guides
  - Be used for non-muscle targets
- EMG: Co-contraction limits accuracy
- E-STIM: Volume conduction targeting errors, pain may require sedation

Alter KE, Karp BI, Toxins 2017, Finlayson H et al Clin Rehabil 2016, Grigorui AI et al, Arch Phys Med Rehabil 2015

US for BoNT Injections: Advantages

- US provides information on muscle
  - Depth
  - Location
  - Thickness
- Anatomic variations, rearrangements
- Safe path to target

US/EMG localization of Longus Colli and Capitis Muscles for Cervical Dystonia

Farrell M, Alter KE et al Toxins 2020

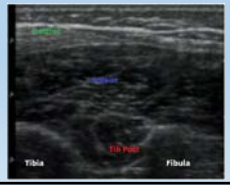
Added Benefits of US Guidance for BoNT Injections

- Multiple approaches to a target muscle, example
  - Tibialis Posterior
    - Antero-medial
    - Anterior
    - Posterior
  - Choice of approaches when
    - Multiple muscles are injected
    - patient positioning is problematic

Antero-medial

Anterior

Posterior



Problematic MOA ✓
Identifiable Goals ✓
Muscle Pattern Identified ✓
Target Muscle Identified ✓
BoNT dose calculated ✓
Now what?

Optimizing muscle targeting

Putting it all Together

Case Studies

Case 1: Common Gait Patterns, Stiff Knee

- Task Specific Runner's dystonia
  - Stiff Knee
    - Limited knee flexion in walking/running
    - Task specific
    - EMG: Rectus firing out of phase
    - Task specific

BoNT Treatment of Common Gait Patterns: Stiff Knee

- Recommendation?
  - BoNT-A injections into rectus femoris

Case 2: 14 Year Old Generalized Dystonia: Focal Problem? Equinus Gait

Treatment Plan?

Severe L ankle equinus

Target muscles: Plantar Flexors and Invertors

Target muscles: Plantar Flexors and Invertors

Tibialis Posterior, posterior medial approach, “Bathtub View”

Tibialis Posterior, posterior lateral approach ”Chair View”

Target muscles: Plantar Flexors and Invertors

Flexor Digitorum Longus, Tibialis Posterior, Anteromedial Approach

Tibialis Anterior, Tibialis Posterior, Anterior Approach

77 y.o. with Post Stroke Spasticity (PSS) and Pain

- CVA 7 years prior to referral
- Referred by OT for spasticity treatment
- Problems?
  - Severe pain R arm/hand limiting ADLs, sleep, hygiene
  - Maceration, skin breakdown in palm
  - ROM restrictions limiting dressing and positioning
  - Unable to tolerate splints or stretching

Video: Initial Assessment

Case : 77 y.o Referred for Assessment of Post Stroke Spasticity (PSS), Left Upper Limb

- EMG guided BoNT injections into:
  - Wrist flexors: FCR, FCU
  - Finger flexors: FDS, FDP, Lumbricals
- Serial casting/splinting
  - 10 days following BoNT injections x 3 weeks with weekly cast changes

Video: Post Treatment Assessment

Ultrasound Guided Botulinum FCR BoNT

Flexor Carpi Radialis Injection, Out of Plane

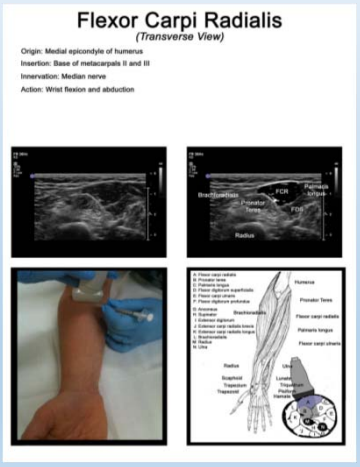


Illustration from Ultrasound Guided Chemodenervation Procedures, Text and Atlas. Demos Medical Publishing

BoNT for Limb Spasticity and Dystonia: Summary

- **A detailed History, Physical and Functional Evaluation will determine**
  - **Should** the patient receive BoNTs?
  - **Which** muscles require treatment
  - **What** is the appropriate dosage/volume?
  - **What** concomitant therapies?
    - BoNT is not administered in insolation
- **BoNT Dosage**
  - Use the lowest effective total dose
    - For large muscles or with spasticity consider increasing volume of dilution/ to enhance spread
- **Instrumented guidance**
  - **Improves toxin efficacy**
  - **Reduces BoNT side effects, procedural risks/complications**
  - For Spasticity in Limb muscles: E-Stim and or US may
    - Improve outcomes
    - Identify specific muscles/muscle fascicles
  - For Dystonia US or EMG or combined US EMG
    - Reduce dysphagia
    - Increases procedural safety
    - Helps determine muscle contribution to an abnormal posture