Guide to Musculoskeletal Injections With Ultrasound
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To my mother, Shamim Agha, who sets the example of the person I want to be—MTA

To Paul D. Murphy, MD and Andrea Murphy—DM
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Foreword

The *Guide to Musculoskeletal Injections With Ultrasound* is a must for clinicians. For too long and in too many studies, we have known that performing injections without guidance results in misplaced and poorly placed treatments and less than optimal results. Given the virtual explosion in the number and types of clinicians using therapeutic injections as an adjunct in the management of musculoskeletal medicine, this cutting-edge manual will quickly fill a vital niche in the clinic. While it can also serve as an excellent teaching tool for academics, it is first and foremost a hands-on tool for the practitioner. Finally, an easy-to-use, illustrated guide is here that allows clinicians to take advantage of ultrasound (US) technology to accurately and efficiently deliver injectate to where it can be most effective. Drs. Agha and Murphy offer a practical approach to using diagnostic US to guide therapeutic injections. From the clear and succinct text to the illustrative photographs, this guide offers readers both a better understanding of US technology and the functional anatomy it reveals. Years of experience and thousands of accurate injections went into the creation of this text, and readers will be able to quickly leverage all this expertise into their day-to-day practice. This guide will serve to accurately answer a key therapeutic question: Am I in the right spot? Given the challenges and complexities of musculoskeletal medicine, clarifying yet another element of the therapeutic approach is invaluable. I would advocate keeping a copy of *Guide to Musculoskeletal Injections With Ultrasound* in every clinic room in your offices.

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Preface

As an attending physician at an academic medical center, I frequently have residents and fellows rotating through my clinics to gain exposure to musculoskeletal ultrasound (US). Most of them want to learn how to do the “textbook” injections under US guidance. Specifically, they were looking for a book that could both help the beginner transition to an intermediate level and also provide the information in a digestible format they could readily use in clinic. With this book, bridging the experience gap is now much easier.

Thus, the goals of this handbook are simple: first, to help those who are new to the world of musculoskeletal US to safely and effectively learn common injections; second, to organize the information such that the reader can quickly access a small detail or read through the full range of specifics contained in an entire section. The content is focused on giving the beginner the knowledge and skills needed to know how to perform an injection in clinic. This handbook makes a process that requires a lot of practice easier, by building confidence, and launching clinicians on the road to proficiency.

This book is not meant to be the end-all of US books or the only tool needed in training; instead, view it as the bridge between your entry into the world of musculoskeletal US and the next level of proficiency. The final step to true expertise will then follow with repetition, practice, and mentorship. Most of the injections outlined in this handbook are commonly performed in musculoskeletal and sports medicine clinics across the United States. The more specialized injections presented at the end of the book on cervical spine and pelvis injections highlight the exciting potential of more advanced interventional musculoskeletal US. All these techniques should be practiced and used with the appropriate level of supervision and mentorship, and I recommend that these more advanced skills be initially done in the setting of fellowship training to ensure that they are taught by experienced practitioners.
The authors and editors are enthusiastic about the use of this handbook to enhance the care of your patients. Dr. Murphy and I look forward to any questions and comments that you may have.

Mohammad Agha, MD, RMSK
Acknowledgments

Anytime a group undertakes a large project such as this one, its success depends on the people involved. My thanks go out to the following people who helped make this book a reality: to my parents, Shamim and Dr. Sirajuddin Agha, who helped make me the person that I am today; to my uncles Dr. Amanullah Pathan and Dr. Karamullah Pathan, for being great role models; to my sisters Lubna, Rafiya, and Iram, and to my wife Aisha, for their support; and to the physicians who helped me get to where I am today: Dr. David Cifu, Dr. William McKinley, Dr. Doug Murphy, Dr. Abu Qutubuddin, and Dr. Robert Rinaldi. I also have to thank Dr. Greg Worsowicz and Dr. James Stannard for their decision to hire me onto the faculty at the University of Missouri. Thank you also to Dr. Ted Choma and Dr. Mark Drymalski for their mentorship. Thank you to Demos Medical Publishing and Beth Barry, who supported this project and helped get it off the ground. And finally, my thanks go out to the authors of each chapter, for helping to make this book a resource for ultrasound practitioners so they can practice medicine at a higher level.
Guide to Musculoskeletal Injections With Ultrasound
CHAPTER 1

Essentials of Musculoskeletal Ultrasound

Mohammad Agha

CHARACTERISTICS OF ULTRASOUND

- An ultrasound (US) wave is generated by a US machine that converts electrical energy to a sound wave at the transducer/gel interface (piezoelectric effect).
- The wave is then propagated through tissue and returns back to the transducer.
- When returning to the transducer, the wave is converted back to electrical energy, producing a US image (reverse piezoelectric effect).
- Multiple outcomes occur when a US wave leaves the transducer:
  1. Refraction: wave direction changes as it passes through fluid.
  2. Reflection: wave hits structure, returning to transducer.
  3. Scatter: Refraction + Reflection away from transducer (1, 2).
  4. Artifacts (see the following).
- Remember that most of the energy from the transducer is lost as dissipated heat.

US TRANSDUCERS

- Linear: good for superficial structures (Figure 1.1).
- Curvilinear: good for curved/deep structures (Figure 1.2).
- Small footprint (“hockey stick”): good for areas of limited contact (wrist, ankle) (Figure 1.3).
- Each probe’s use is dependent on the depth of structure of interest.
• Linear probes have high frequency (typically >10 MHz), which provides high resolution, but low penetration/depth (up to 6 cm).
• Curvilinear probes have lower frequencies, which provide lower resolution, but increased penetration/depth (for structures such as the hip) (2).

Figure 1.1 Linear probe: L4-12t-RS LoQG e wide band linear array probe with 4.2–13 MHz frequency. Courtesy of GE.

Figure 1.2 Curvilinear probe: C1-5-RS LOGIQ e wide band convex array probe with 2–5 MHz frequency. Courtesy of GE.
SCANNING TECHNIQUE

- Position the US machine near patient for maximal viewing area.
- Hold the probe between your thumb and finger of your dominant hand.
- Be sure to wrap your entire hand around the probe, with the end of the probe near the fifth digit.
- Maintain scanning hand contact with patient at all times while scanning—it increases stability when scanning and injecting a patient.
- Keep your scanning hand lower than your shoulder.
- Keep your elbow close to your body.
- Can perform two techniques with probe to improve image resolution.
  - Heel-toe: moving the probe long-axis.
  - Toggling: moving probe short-axis.

ARTIFACTS

- Anisotropy: when the sound wave is not perpendicular to object of interest, the imaging trait of the tissue (when off as little as 5°) is lost. This typically results in darkening of tissue, mimicking pathology.
• Shadowing: US beam is refracted, reflected, or absorbed, causing an anechoic (black) image deep to the object (typically beneath bone, with gas, or deep to a calcification).
• Posterior acoustic shadowing: soft tissue deep to an object is hyperechoic (brighter) compared to adjacent soft tissue. Typically occurs with presence of fluid or solid soft tissue tumor.
• Posterior reverberation: a smooth/flat object reflects the sound beam back and forth between itself and the transducer, causing linear echoes deep to the structure. If it continues deeper, called ring-down artifact (associated with metal).
• Comet tail: deep hyperechoic echoes due to soft tissue gas.
• Beam width artifact: beam too wide relative to imaged object. Corrected by adding focal zone (see the following) to level of object (1).

DOPPLER

• Doppler effect: color flow changes as object moves toward or away from an object.
• Color flow: colored blood flow indicating direction of blood flow (red: toward transducer; blue: away).
• Duplex Doppler: US + waveform recorded.
• Power Doppler: sensitive to blood flow and transducer movement, but does not provide directional information.
• Increased flow on power Doppler can indicate inflammation, increased perfusion, or neovascularization.
• Power Doppler can also help with identifying other structures.
• Mass with flow generally indicates malignancy, compared to mass without flow, which generally indicates benign; mass (always biopsy to be sure).
• Lymph node: no flow/hilar flow: generally benign; spotted/peripheral/mixed flow: generally malignant (again, biopsy to be sure).
• Complex fluid versus synovitis.
• Complex fluid: no internal flow on power Doppler.
• Synovitis: increased flow (1).

US PROBE CHARACTERISTICS

Linear: high frequency (>10 MHz), better resolution, less depth (Table 1.1).
Curvilinear: lower frequency (2–5 MHz), decreased resolution, increased depth (Table 1.2).
Hockey stick: high frequency (>10 MHz), increased resolution, less depth, best for smaller structures.

**IMAGE OPTIMIZATION**

1. Select the *proper transducer*.
2. Adjust *focal zones* to improve brightness at the level of the object of interest (only add minimum number needed; otherwise it reduces frame rate).
3. Adjust *gain* for appropriate overall brightness on screen to identify local structures.
4. Adjust *depth gain/time gain compensation* to add brightness at specific area of screen (3).

The image produced has objects with difference intensities:
- Hyperechoic: object brighter than surrounding objects (ligament, tendon, bone, calcification).
- Hypoechoic: object darker than surrounding structures (fluid, tendinosis, tear).
- Isoechoic: object has equal brightness in relation to surrounding structures.
- Anechoic: object/area dark (black) (2) (blood vessel, fluid, cartilage).

**Table 1.1 Advantages of Ultrasound**

<table>
<thead>
<tr>
<th>Advantage</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-resolution images</td>
</tr>
<tr>
<td>Real-time imaging</td>
</tr>
<tr>
<td>Dynamic examination</td>
</tr>
<tr>
<td>Procedure guidance</td>
</tr>
<tr>
<td>Can compare contralaterally</td>
</tr>
<tr>
<td>No radiation</td>
</tr>
<tr>
<td>Portable</td>
</tr>
<tr>
<td>No known contraindications</td>
</tr>
<tr>
<td>Relatively inexpensive</td>
</tr>
</tbody>
</table>
Individual musculoskeletal structures each have defined intensity characteristics. Note again that these terms describe object intensity relationships relative to surrounding structures. Therefore, objects that are hyperechoic in one image can be hypoechoic (relative to another structure) in another image.

**APPEARANCE OF NORMAL STRUCTURES UNDER ULTRASOUND** (4)

- **Tendon**: hyperechoic, linear, fibrillar
- **Ligament**: hyperechoic, linear, fibrillar, more compact than tendon
- **Muscle**: relatively hypoechoic, with hyperechoic fascial planes
- **Bone**: hyperechoic interface, anechoic deep to bone
- **Hyaline cartilage**: hypoechoic, uniform
- **Fibrocartilage**: hyperechoic
- **Peripheral nerve**: fascicular appearance, with hypoechoic nerve fascicles, and hyperemic connective tissue epineurium (3)

**INJECTATES**

**Corticosteroids**

- Natural substance formed in the adrenal cortex.
- Mechanism of action: down-regulate immune function; inhibit cell-mediated immunity; alter mRNA production, altering protein annexin-I.
- Have mineralcorticoid (water/electrolyte) and glucocorticoid (metabolism/inflammatory) properties.
- Steroids can be soluble or insoluble, meaning some have esters (water insoluble), causing them to form microcrystals.
• Betamethasone and dexamethasone do NOT have esters, thus they are broken down via hydrolysis by the body’s cell esterases.
• This leads to longer effect in joint.
• Esters have quicker onset, but decreased duration (Table 1.3, Table 1.4).

Table 1.3 Commonly Injected Corticosteroids

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Equivalent Potency</th>
<th>% Particles &gt;10 µm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone acetate</td>
<td>4</td>
<td>45</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>4</td>
<td>45</td>
</tr>
<tr>
<td>Betamethasone acetate/sodium phosphate</td>
<td>0.75</td>
<td>35</td>
</tr>
<tr>
<td>Dexamethasone sodium phosphate</td>
<td>0.75</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1.4 Different Steroid Doses for Variably Sized Joints (5)

<table>
<thead>
<tr>
<th>Joint Size</th>
<th>Methylprednisolone Acetate (mg)</th>
<th>Triamcinolone Acetate (mg)</th>
<th>Betamethasones (mg)</th>
<th>Dexamethasone Sodium Phosphate (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large</td>
<td>20–80</td>
<td>10–15</td>
<td>1–2</td>
<td>2–4</td>
</tr>
<tr>
<td>Medium</td>
<td>10–40</td>
<td>5–10</td>
<td>0.5–1.0</td>
<td>2–3</td>
</tr>
<tr>
<td>Small</td>
<td>4–10</td>
<td>2.5–5</td>
<td>0.25–0.5</td>
<td>0.8–1</td>
</tr>
</tbody>
</table>


ADVERSE EFFECTS

• Septic arthritis
• Postinjection flare (most common adverse effect, develops in a few hours, lasts 2–3 days)
• Local tissue atrophy
• Tendon rupture
• Cartilage damage
• Facial flushing
• Chills/shakes/headache (histamine release from steroid)
• Increased blood glucose levels
• Local tissue necrosis
• Calcification
• Skin atrophy/depigmentation

ADVERSE CENTRAL NERVOUS SYSTEM EFFECTS

• Tetraplegia/paraplegia
• Can be due to brain/spinal cord infarction, vascular injury, embolism from steroid particulate (most likely), neurotoxicity from preservative (benzyl alcohol), or drug vehicle (polyethylene glycol)

CONTRAINDICATIONS FOR CORTICOSTEROID INJECTIONS

• Absolute: Sepsis (systemic/intra-articular), intra-articular fracture, and joint instability.
• Relative: Juxta-articular osteoporosis, coagulopathy, joint injection more than three times per year, or one injection in the last 6 weeks.

LOCAL ANESTHETICS (TABLE 1.5)

• Inhibit nerve excitation through sodium channel blockade at cell membrane (inhibits action potential).
• Effective analgesic due to blocking smaller diameter nerves (ie, pain fibers).
• Two categories: amides (lidocaine) and esters.
• Can be administered with vasoconstrictor to decrease vascular absorption, increasing duration.
• Anesthetic characteristics determined by acid dissociation $pK_a$, lipid solubility, protein binding.
• $pK_a$: onset of action.
• Lipid solubility: nerve membrane penetration (higher solubility: higher penetration).
• Protein binding: duration of action.

**Table 1.5 Commonly Used Local Anesthetics**

<table>
<thead>
<tr>
<th>Generic Name (min)</th>
<th>Relative Potency</th>
<th>Onset</th>
<th>Duration of Action (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procaine hydrochloride</td>
<td>1</td>
<td>Moderate</td>
<td>30–60</td>
</tr>
<tr>
<td>Lidocaine hydrochloride</td>
<td>2</td>
<td>Rapid</td>
<td>80–120</td>
</tr>
<tr>
<td>Ropivacaine hydrochloride</td>
<td>6</td>
<td>Moderate</td>
<td>140–200</td>
</tr>
<tr>
<td>Bupivacaine hydrochloride</td>
<td>8</td>
<td>Long (2–10 min)</td>
<td>180–360</td>
</tr>
</tbody>
</table>

**Contraindications**

• Sensitivity to amide anesthetic
• Local infection
• Coagulopathy
• Epinephrine use if patient uses monoamine oxidase (MAO) inhibitor/tricyclic antidepressants (TCA) (prolonged hypertension).

**Adverse Side Effects**

• Central nervous system: shivering, muscle twitches, tremor, hypoventilation, and convulsions.
• Cardiac: arrhythmias, cardiovascular (CV) depression/collapse.
• Anaphylaxis: loss of consciousness, convulsions, and CV effects.
• Skeletal muscle toxicity: necrosis, cell apoptosis due to permanent intracellular calcium, muscle weakness, and chondrocyte toxicity.
• Platelets have alpha granules that release growth factors.
• These growth factors are small peptides that bind membrane receptors and promote downstream pathways.
• Also mediate chemotaxis and cell migration through “chemical mediators.”
• Can also affect mitosis, angiogenesis, and cell differentiation.
• Platelet-rich plasma (PRP) prepped from autologous whole blood.
• Spun down by centrifuge to produce three layers:
  1. plasma layer (top)
  2. platelets and white blood cells (WBC)
  3. red blood cells
• Middle layer (PRP) suctioned out; can add calcium chloride or thrombin to activate platelets.
• This releases 70% growth factors in 10 minutes.
• It’s believed that needling the structure of interest causes focal bleeding and acute inflammatory response, aiding cell recruitment and repair.

**VARIOUS BLOOD PRODUCTS**

• Autologous conditioned serum: whole blood drawn into glass beads to start monocyte activation.
• Autologous plasma rich in growth factors (PRGF): venous blood collected in 5 mL tubes with 3.8% trisodium citrate, centrifuged at 1,800 rpm for 8 minutes. 0.25 to 1 mL fraction transferred to sterile tubes. Calcium added, forming fibrin matrix with platelets.
• Autologous conditioned plasma: whole blood centrifuged to form PRP, then placed into bottle with calcium chloride in centrifuge to produce platelet fibrin matrix.
• Platelet leukocyte-rich gel: centrifuge whole blood to produce PRP and leukocyte-rich plasma (top layer), which are mixed together with thrombin or calcium chloride to form a gel. It is thought that adding WBCs confers antibacterial properties.
• Autologous blood injections: whole venous blood mixed with lidocaine or bupivacaine for injection.
STEM CELLS

- Three basic categories: embryonic, adult (mesenchymal), and induced pluripotent.
- Most studied: mesenchymal stem cells.
- Isolated from many tissues (bone marrow, muscle adipose).
- The closer a tissue is to cell line of desired tissue, the more effective at differentiating into desired cell line.
- Cells can be used from cultured lines or same-day sample.

To Culture Stem Cells

- Seed cells onto monolayer flask
- Attach to surface
- Adherent cells get culture medium to grow
- Growth continues until cells touch each other
- Once they touch they stop growing (confluence)
- Cells are then placed into another flask and medium (passage)

Same-Day Use

- Harvest tissue from adipose
- Release cells or get fraction by breaking down collagen matrix to centrifuge cells

Mechanisms of Action

- Cell differentiation
- Paracrine effects (chemokine secretion, suppressed dendritic cells, reduced effector T cells/NK cells/MHC Class II cells)
- Macrophage deactivation (prevents further metabolism)

Autologous vs. Allogeneic Cell Lines

- Autologous: carry more genetic variants; decreased differentiation if older patients.
- Allogeneic: mass production possible; can activate host immune system (IL-6 deregulation).
• Administration of stem cells regulated by Food and Drug Administration (FDA) (FDA Tissue Regulation, 21 CFR Part 1271) (8).
• FDA does not allow extended ex vivo culturing of growth factors, and only allows “minimally manipulated tissue” (8).
REFERENCES