

Submission ID #: 71239

Scriptwriter Name: Pallavi Sharma

Project Page Link: <https://review.jove.com/account/file-uploader?src=21727943>

Title: Patient-Specific Electric Field Simulation in Spinal Metastasis Electrochemotherapy

Authors and Affiliations:

Paul Beunon¹, Baptiste Bonnet¹, Lambros Tselikas¹, Paul Janvier¹, Genti Xhepa¹, Olivier Sutter^{2,3}, Baudouin Denis de Senneville⁴, Luc Lafitte⁴, Olivier Seror^{2,3}, Lluís M. Mir⁵, Frederic Deschamps¹, Clair Poignard³

¹Department of Anesthesiology, Surgery and Interventional Radiology, Gustave Roussy

²Interventional Radiology Department, Avicenne Hospital

³AIMOKA : Inria, Assistance Publique Hôpitaux de Paris, Université Sorbonne Paris Nord

⁴CNRS, INRIA, University of Bordeaux

⁵UMR 9018 METSY, Université Paris-Saclay, CNRS, Gustave Roussy

Corresponding Authors:

Beunon Paul (paul.beunon@gustaveroussy.fr)

Email Addresses for All Authors:

Baptiste Bonnet	(baptiste.bonnet@gustaveroussy.fr)
Lambros Tselikas	(lambros.tselikas@gustaveroussy.fr)
Paul Janvier	(paul.janvier@gustaveroussy.fr)
Genti Xhepa	(genti.xhepa@gustaveroussy.fr)
Olivier Sutter	(olivier.sutter@aphp.fr)
Baudouin Denis de Senneville	(baudouin.denis-de-senneville@inria.fr)
Luc Lafitte	(luc.lafitte@inria.fr)
Olivier Seror	(olivier.seror@aphp.fr)
Lluís M. Mir	(luís.mir@cnrs.fr)
Frederic Deschamps	(frederic.deschamps@gustaveroussy.fr)
Clair Poignard	(clair.poignard@inria.fr)
Beunon Paul	(paul.beunon@gustaveroussy.fr)

Author Questionnaire

- 1. Microscopy:** Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No.**

- 2. Software:** Does the part of your protocol being filmed include step-by-step descriptions of software usage? **Yes**

- 3. Filming location:** Will the filming need to take place in multiple locations? **No.**

- 4. Testimonials (optional):** Would you be open to filming two short testimonial statements **live during your JoVE shoot**? These will **not appear in your JoVE video** but may be used in JoVE's promotional materials. **Yes**

Current Protocol Length

Number of Steps: 38

Number of Shots: 57

Introduction

Videographer: Obtain headshots for all authors available at the filming location.

INTRODUCTION:

~~REQUIRED: Summarize your research focus and the main questions it aims to answer.~~

- 1.1. **Paul Beunon:** Our protocol simulates patient-specific electric fields during spinal electrochemotherapy and compares them with post-treatment tumor necrosis.
 - 1.1.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B roll: 7.4.1*

~~Describe the research gap or limitation in existing methods and how this protocol addresses them.~~

- 1.2. **Paul Beunon:** Existing workflows rarely validate simulated electric fields against three-dimensional treatment response in spinal metastatic disease.
 - 1.2.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

CONCLUSION:

~~Describe the most important consideration or challenge when performing this protocol.~~

- 1.3. **Paul Beunon:** The main challenge is identifying the relevant isodose threshold for each treatment, organ, and clinical setting.
 - 1.3.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B roll: 6.3.2*

~~Are there any additional methods or analyses that can be performed following this procedure?~~

- 1.4. **Paul Beunon:** Additional analyses can test automated segmentation, registration uncertainty, and dose-response relationships across electric-field thresholds.

- 1.4.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

~~How can future studies build on this work? Describe the questions or research directions that can be investigated next.~~

- 1.5. **Paul Beunon:** Future studies should validate these early findings in larger spinal metastasis cohorts and other electrochemotherapy indications.

- 1.5.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

Videographer: Obtain headshots for all authors available at the filming location.

Testimonial Questions (OPTIONAL):

Videographer: Please capture all testimonial shots in a wide-angle format with sufficient headspace, as the final videos will be rendered in a 1:1 aspect ratio. Testimonial statements will be presented live by the authors, sharing their spontaneous perspectives.

What problem in your field of research does your JoVE article address?

- 1.6. **Paul Beunon, MD, MSc, Interventional Radiologist:** (authors will present their testimonial statements live)

- 1.6.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

What is the key takeaway you hope viewers remember after watching your video article?

- 1.7. **Paul Beunon, MD, MSc, Interventional Radiologist:** (authors will present their testimonial statements live)

- 1.7.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

Ethics Title Card

This research has been approved by the Institutional Review Board at Université Paris-Saclay

Protocol

***Videographer:** Please always record an audio slate while filming each shot mentioned in the shotlist.*

2. Anatomical Segmentation on Initial CT (CTi)

Demonstrator: Paul Beunon

- 2.1. After importing the data into 3D slicer and setting CTi (*C-T-I*) as the reference volume [1], open the Segment Editor module and create a segment named Cortical bone [2]. Use the **Threshold** tool in CTi to isolate high-density cortical bone, then manually refine the segment using the Scissors or Paint tools as needed [3].
 - 2.1.1. WIDE: Talent in front of the computer with the software window displayed on the screen
 - 2.1.2. SCREEN: 2.1.2.mp4: 00:02-00:15
 - 2.1.3. SCREEN: 2.1.3.mp4: 00:02-00:20, 00:30-00:39.
- 2.2. Create a segment named Fat. Use the **Threshold** tool to select low-density fat in the perirenal or subcutaneous space [1].
 - 2.2.1. SCREEN: 2.2.1.mp4: 00:02-00:06, 00:13-00:19, 00:25-00:33
- 2.3. Next, construct an intervertebral disc segment and use the 3D Paint tool on axial, sagittal, and coronal views [1]. Check **Paint outside existing segments** to restrict painting to empty voxels and avoid overwriting existing segments [2].
 - 2.3.1. SCREEN: 2.3.1.mp4; 00:08-00:12, 00:17-00:39
 - 2.3.2. SCREEN: 2.3.2.mp4.
- 2.4. Then, set up a Cancellous bone segment for vertebral cancellous bone [1]. Use the 3D Paint tool to fill the internal trabecular compartments. Select the **paint outside existing segments** as described previously [2].
 - 2.4.1. SCREEN: 2.4.1.mp4: 00:05-00:20
 - 2.4.2. SCREEN: 2.4.2.mp4: 00:08-00:24, 00:44-00:48
- 2.5. Create a segment labeled Spinal cord [1] and use the 3D Paint tool to manually contour the cord on axial slices from above to below the treated levels [2].
 - 2.5.1. SCREEN: 2.5.1.mp4: 00:05-00:15
 - 2.5.2. SCREEN: 2.5.2.mp4 00:08-00:28.
- 2.6. Next, define a segment named Cerebro-spinal fluid. Use the 3D Paint tool to fill the cerebrospinal fluid space surrounding the spinal cord within the thecal sac [1]. Check **Paint outside existing segments** to avoid overwriting existing segments [2].

- 2.6.1. SCREEN: 2.6.1.mp4: 00:04-00:08, 00:21, 00:34-00:45
- 2.6.2. SCREEN: 2.6.2.mp4: 00:04-00:07
- 2.7. Create additional segments for cement, coils, or lungs if present [1]. Use the **Threshold** tool to identify hyperdense cement or coils and hypodense lung parenchyma. Perform manual correction as needed [2].
 - 2.7.1. SCREEN: 2.7.1.mp4: 00:04-end
 - 2.7.2. SCREEN: 2.7.2.mp4: 00:25-00:45.
- 2.8. Save the updated Slicer scene [1].
 - 2.8.1. SCREEN: 2.8.1.mp4: 00:02-00:06 -

3. MRI Fusion and Tumor Segmentation

- 3.1. Import the pre-procedural MRI volume MRIp (*M-R-I-P*) into the Slicer scene [1].
 - 3.1.1. SCREEN: 3.1.1.mp4: 00:02-00:10
- 3.2. Use the **Transforms** module to perform rigid registration of MRIp onto CTi using vertebral osseous landmarks at the treated level to guide registration [1].
 - 3.2.1. SCREEN: 3.1.2.mp4: 00:14-00:19, 00:31-00:34, 00:40-00:46, 03:20-03:29
- 3.3. Apply the transform to MRIp and visually assess co-registration in axial and sagittal planes [1]. Accept the registration only if the visual alignment and target registration error are less than 2.5 millimeters [2].
 - 3.3.1. SCREEN: 3.3.1.mp4: 00:21-00:40
 - 3.3.2. SCREEN: 3.3.2.mp4: 00:26-00:40
- 3.4. Then, create a new segment named Tumor [1]. Use the **Paint** tool on MRIp to manually delineate epidural and vertebral tumor involvement at baseline [2].
 - 3.4.1. SCREEN: 3.4.1.mp4: 00:03-00:07
 - 3.4.2. SCREEN: 3.4.2.mp4: 00:05-00:18, 00:29-00:38
- 3.5. Apply optional smoothing to the Tumor segment to obtain a coherent three-dimensional volume without gaps [1] and save the updated Slicer scene [2].
 - 3.5.1. SCREEN: 3.5.1.mp4: 00:21-00:32, 00:52-01:00
 - 3.5.2. SCREEN: 3.5.2.mp4: 00:02-00:07

4. CT with Needle Fusion and Electrode Definition in AI4DEEP

- 4.1. Import the intra-procedural computed tomography volume with needles CTa into the 3D Slicer scene [1].
 - 4.1.1. SCREEN: 4.1.1.mp4.

- 4.2. Utilize the Transforms module for rigid registration of CTa onto Cti [1]. Employ the same vertebral bony landmarks as in the previous step to ensure proper alignment.[2].

4.2.1. SCREEN: 4.2.1.mp4: 00:48-01:00

4.2.2. SCREEN: 4.2.2.mp4: 01:06-01:18

- 4.3. Launch the AI4DEEP (*A-I-Four-Deep*) module and create one virtual needle for each electrode, starting from the active electrode tip [1].

4.3.1. SCREEN: 4.3.1.mp4: 00:08-00:16, 01:12-01:20

- 4.4. Verify in axial, coronal, and sagittal views that each Electrode number matches accurately with a single physical active tip [1].

4.4.1. SCREEN: 4.4.1.mp4: 00:05-00:08, 00:27-00:39, 01:55-01:59

- 4.5. Save the updated scene containing anatomical structures, tumor segmentation, and electrode geometry [1].

4.5.1. SCREEN: 4.5.1.mp4: 00:04-00:11

5. Tissue Mapping and Electrode Parameter Setup in AI4DEEP

- 5.1. In the AI4DEEP interface, assign each anatomical segment to a corresponding tissue class with predefined electrical conductivity [1].

5.1.1. SCREEN: 5.1.1.mp4: 00:04-00:26

- 5.2. Set the default background tissue to muscle conductivity so that all non-segmented voxels are treated as muscle [1].

5.2.1. SCREEN: 5.2.1..mp4

- 5.3. Verify in the AI4DEEP summary panel that each segment is aligned with the expected tissue type and conductivity, then save the configuration [1].

5.3.1. SCREEN: 5.3.1.mp4: 00:12-00:39

- 5.4. In the AI4DEEP interface, specify the active tip length for each electrode according to the clinical procedure [1] and set the electrode diameter to 1.8 millimeters [2].

5.4.1. SCREEN: 5.4.1.mp4

5.4.2. SCREEN: 5.4.2.mp4: 00:08-00:13

- 5.5. Enter the clinically applied electric field amplitude in volts per centimeter [1].

5.5.1. SCREEN: 5.5.1.mp4: 00:52-01:00

- 5.6. Then, define the electrode pairs that were activated during the treatment [1].

5.6.1. SCREEN: 5.6.1.mp4; 00:06-00:15

- 5.7. Let AI4DEEP compute the applied voltage for each electrode pair based on the inter-electrode distance while ensuring the requested voltage-to-distance ratio in volts per

centimeter is respected [1].

5.7.1. SCREEN: 5.7.1.mp4: 00:07-00:30

- 5.8. Set the number of pulses to 8 and the pulse duration to 100 microseconds according to the clinical protocol [1]. Then, save the AI4DEEP configuration [2].

5.8.1. SCREEN: 5.8.1.mp4: 00:04-00:12

5.8.2. SCREEN: 5.8.2.mp4: 00:02-00:07.

6. Electric Field Simulation and Isodose-Based Tumor Coverage Analysis

- 6.1. In the AI4DEEP interface, start the electrostatic field computation using the configured anatomy, conductivities, and electrode parameters [1].

6.1.1. SCREEN: 6.1.1.mp4: 00:02-00:06

- 6.2. Once the software generates the geometrical configuration and solves the linear electrostatic potential, save the simulation output and the updated Slicer scene [1].

NOTE: The VO is edited for the deleted shot

~~6.2.1. SCREEN: Show the computation process running in the AI4DEEP interface.~~ **NOTE: Not filmed.**

6.2.2. SCREEN: 6.2.2.mp4:

- 6.3. In the AI4DEEP interface, select the option to generate electric field isosurfaces from the simulated field [1]. Select a range of isodose thresholds and generate the corresponding three-dimensional isodose maps [2].

6.3.1. SCREEN: 6.3.1.mp4: 00:03-end

6.3.2. SCREEN: 6.3.2.mp4: 00:06-00:30.

- 6.4. Display individual isodose maps in a three-dimensional view to observe the spatial field distribution [1]. The field typically ranges from pale yellow at low amplitudes to red at high amplitudes [2].

6.4.1. SCREEN: 6.4.1.mp4: 00:18-00:40

6.4.2. SCREEN: 6.4.2.mp4: 00:22-00:32

- 6.5. For each isodose, record the percentage of tumor coverage values automatically computed based on the overlap between the isodose volume and the Tumor segmentation [1].

6.5.1. SCREEN: 6.5.1.mp4

- 6.6. Save all isodose segments or models and the tumor coverage values for subsequent analysis [1].

6.6.1. SCREEN: 6.6.1.mp4: 00:03-00:13

7. Post-Procedural MRI Selection and Necrosis Segmentation

- 7.1. Perform follow-up MRI at 6 weeks after electrochemotherapy and every 2 months thereafter [1]. Select the MRI scan showing the largest necrotic volume or best radiological response for segmentation to account for heterogeneous and delayed treatment response [2].
 - 7.1.1. SCREEN: 7.1.1.mp4: 00:14-00:30
 - 7.1.2. SCREEN: 7.1.2.mp4: 00:10-00:30.
- 7.2. Import the post-treatment contrast-enhanced T1 fat-suppressed axial sequence centered on the treated levels MRIs into 3D Slicer [1].
 - 7.2.1. SCREEN: 7.2.1.mp4: 00:05-00:25
- 7.3. Perform rigid registration of MRIs onto CTi using the same predefined vertebral landmarks as used previously [1]. Apply the transform, calculate the target registration error using the same reference landmarks, and confirm that it is less than or equal to 2.5 millimeters to document registration accuracy [2].
 - 7.3.1. SCREEN: 7.3.1.mp4: 00:04-00:1, 00:14-00:19, 00:23-00:27, 02:39-02:42
 - 7.3.2. SCREEN: 7.3.2.mp4: 00:03-00:35.
- 7.4. Create a new segment named Tumor necrosis [1]. Use the **Paint** tool to manually delineate the non-enhancing necrotic portion of the tumor on the post-electrochemotherapy magnetic resonance imaging slice by slice [2].
 - 7.4.1. SCREEN: 7.4.1.mp4: 00:16-00:21
 - 7.4.2. SCREEN: 7.4.2.mp4: 01:16-01:17, 01:35-01:54
- ~~7.5. When multiple follow-up MRI datasets are available, select the examination demonstrating the largest necrotic volume or best radiological response and use this dataset for segmentation [1].~~
 - ~~7.5.1. SCREEN: Show comparison of multiple follow-up MRIs with selection of the optimal dataset. NOTE: Not filmed~~
- 7.6. Apply optional smoothing to the Tumor necrosis segment to obtain a coherent contiguous volume [1]. Then, perform a quantitative comparison between the simulated field and necrosis [2].
 - 7.6.1. SCREEN: 7.6.2.mp4
 - 7.6.2. Talent at the computer screen showing the simulated field and necrosis plots.

Results

8. Results

- 8.1. Mean Dice similarity coefficients showed a bell-shaped relationship across the cohort [1]. The values peaked between 160 and 200 volts per centimeter [2], and tumor coverage gradually declined as thresholds increased [3].
 - 8.1.1. LAB MEDIA: Figure 2.
 - 8.1.2. LAB MEDIA: Figure 2. *Video editor: Highlight the red line around the 160 to 200 volts per centimeter marks*
 - 8.1.3. LAB MEDIA: Figure 2. *Video editor: Highlight the blue line labeled "Tumor coverage," showing it moving downward from left to right*
- 8.2. Marked heterogeneity was observed between cases, with Best Dice values ranging from 0.0156 to 0.7684 [1] and corresponding Best Iso values ranging from 100 to 500 volt per centimeter [2].
 - 8.2.1. LAB MEDIA: Figure 3. *Video editor: Show the spread of different colored lines across the graph.*
 - 8.2.2. LAB MEDIA: Figure 3. *Video editor: Highlight the full horizontal axis from 100 to 500 volt per centimeter.*
- 8.3. A representative overlay showed spatial correspondence between post-treatment tumor necrosis [1] and the 200 volt per centimeter isodose volume [2].
 - 8.3.1. LAB MEDIA: Figure 4. *Video editor: Highlight the green shaded region labeled necrosis.*
 - 8.3.2. LAB MEDIA: Figure 4. *Video editor: Highlight the yellow shaded region labeled 200 volt per centimeter.*
- 8.4. The first electrochemotherapy session showed limited necrosis [1], whereas a second procedure demonstrated substantially increased tumor coverage at 200 volts per centimeter [2].
 - 8.4.1. LAB MEDIA: Figure 5. *Video editor: Highlight figure A and B.*
 - 8.4.2. LAB MEDIA: Figure 5. *Video editor: Highlight figure C and D*
- 8.5. The 300 volt per centimeter isodose extended into the right S1 foramen [1], while the contralateral root remained outside the high-field region [2].
 - 8.5.1. LAB MEDIA: Figure 6. *Video editor: Highlight the orange region extending into the right side near the S1 roots label.*
 - 8.5.2. LAB MEDIA: Figure 6. *Video editor: Highlight the opposite side where no orange*

region is present.

1. Cortical
Pronunciation link: <https://www.merriam-webster.com/dictionary/cortical>
IPA: /'kɔr.tə.kəl/
Phonetic Spelling: kor·tuh·kuhl
2. Perirenal
Pronunciation link: <https://www.merriam-webster.com/dictionary/perirenal>
IPA: /,per.ə'ri:.nəl/
Phonetic Spelling: pehr·uh·ree·nuhl
3. Intervertebral
Pronunciation link: <https://www.merriam-webster.com/dictionary/intervertebral>
IPA: /,ɪn.tə'vɜ:.tə.brəl/
Phonetic Spelling: in·ter·vur·tuh·bruhl
4. Cancellous
Pronunciation link: <https://www.merriam-webster.com/dictionary/cancellous>
IPA: /kæn'sel.əs/
Phonetic Spelling: kan·sel·uhs
5. Vertebral
Pronunciation link: <https://www.merriam-webster.com/dictionary/vertebral>
IPA: /'vɜ:.tə.brəl/
Phonetic Spelling: vur·tuh·bruhl
6. Trabecular
Pronunciation link: <https://www.merriam-webster.com/dictionary/trabecular>
IPA: /trə'bek.jə.lə/
Phonetic Spelling: truh·bek·yuh·ler
7. Spinal
Pronunciation link: <https://www.merriam-webster.com/dictionary/spinal>
IPA: /'spaɪ.nəl/
Phonetic Spelling: spy·nuhl
8. Cerebrospinal
Pronunciation link: <https://www.merriam-webster.com/dictionary/cerebrospinal>
IPA: /sə'ri:.broʊ'spaɪ.nəl/
Phonetic Spelling: suh·ree·broh·spy·nuhl
9. Thecal
Pronunciation link: <https://www.merriam-webster.com/dictionary/thecal>
IPA: /'θi:.kəl/
Phonetic Spelling: thee·kuhl
10. Parenchyma
Pronunciation link: <https://www.merriam-webster.com/dictionary/parenchyma>
IPA: /pə'reŋ.kə.mə/
Phonetic Spelling: puh·reng·kuh·muh
11. Procedural
Pronunciation link: <https://www.merriam-webster.com/dictionary/procedural>
IPA: /prə'si:.dʒə.əl/
Phonetic Spelling: pruh·see·jer·uhl

12. Osseous
Pronunciation link: <https://www.merriam-webster.com/dictionary/osseous>
IPA: /'ɑ:.si.əs/
Phonetic Spelling: ah·see·uhs
13. Registration
Pronunciation link: <https://www.merriam-webster.com/dictionary/registration>
IPA: /,redʒ.ə'streɪ.fən/
Phonetic Spelling: rej·uh·stray·shuhn
14. Delineate
Pronunciation link: <https://www.merriam-webster.com/dictionary/delineate>
IPA: /dɪ'lm.i.ert/
Phonetic Spelling: dih·lin·ee·ayt
15. Epidural
Pronunciation link: <https://www.merriam-webster.com/dictionary/epidural>
IPA: /,ep.ə'dʊr.əl/
Phonetic Spelling: ep·uh·door·uhl
16. Electrostatic
Pronunciation link: <https://www.merriam-webster.com/dictionary/electrostatic>
IPA: /ɪˌlek.troʊ'stæt.ɪk/
Phonetic Spelling: ih·lek·troh·stat·ik
17. Isodose
Pronunciation link: <https://www.merriam-webster.com/dictionary/isodose>
IPA: /'aɪ.sə.doʊs/
Phonetic Spelling: eye·suh·dohs
18. Necrosis
Pronunciation link: <https://www.merriam-webster.com/dictionary/necrosis>
IPA: /nə'kroʊ.sɪs/
Phonetic Spelling: nuh·kroh·suhs
19. Radiological
Pronunciation link: <https://www.merriam-webster.com/dictionary/radiological>
IPA: /,reɪ.di.ə'lɑ:.dʒɪ.kəl/
Phonetic Spelling: ray·dee·uh·loj·i·kuhl
20. Heterogeneity
Pronunciation link: <https://www.merriam-webster.com/dictionary/heterogeneity>
IPA: /,het.ə.ʊʊ.dʒə'ni:.ə.ti/
Phonetic Spelling: het·uh·roh·juh·nee·uh·tee