Contribution of Bone Scintigraphy in Benign Bone Pathology: Illustrations of Cases from the Nuclear Medicine Department at the University Hospital of Fes

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Abstract

This work provides an overview of the effectiveness of bone scintigraphy and its role in diagnosing various benign conditions in the Nuclear Medicine Department of the University Hospital of Fez. It analyzes the criteria for selecting scintigraphy as a diagnostic tool and outlines the principles, key features, and protocols involved. These details support clinicians in confirming their diagnostic reasoning when evaluating musculoskeletal lesions or bone abnormalities, guiding their choice of imaging modalities.

Clinicians initiate the diagnostic process by identifying relevant clinical factors and areas of uncertainty, leading to a preliminary diagnosis. Subsequently, nuclear physicians tailor the scintigraphy examination to address the specific clinical concerns. It’s important to note that the clinical cases presented serve as illustrative examples rather than definitive benchmarks for image quality or equipment settings. They are intended to stimulate individual reflection based on each unique clinical scenario.

Fig. 9 Early and late whole body scan. Polyostotic Fibrous Bone Dysplasia.

Keywords: Bone scintigraphy; benign bone pathology; hybrid SPECT/CT; topographical diagnosis, quantification and monitoring of bone lesions.

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Introduction

Bone scintigraphy (BS) is the diagnostic test most frequently performed in single-photon nuclear medicine. It is one of several diagnostic algorithms whose characteristics (reliability, sensitivity, specificity, positive predictive value and negative predictive value) have long been well known for the various pathologies in which it is used (1).

Analysis of planar bone scans focuses on the appearance, number and location of fixation anomalies. SPECT-CT locates and specifies fixation anomalies and correlates them with morphological lesions that may be suggestive of a given pathology. Subsequent morphological investigations (multi-slice CT, MRI), 18F-fluorodeoxyglucose positron emission tomography, serology, bacterial cultures or osteomedullary biopsy may be required to diagnose and assess the condition (2).

Principle of bone scintigraphy

This isotopic imaging test, which is widely used in current practice, enables the metabolism of all bone segments to be analysed. It involves the intravenous administration of an osteotropic radiotracer, consisting of a vector and a radioisotope: most commonly methylene diphosphonate (99mTc-MDP), which was evaluated and marketed in the mid-1970s, and which binds to the skeleton in proportion to local blood flow and bone remodelling activity (4). Detection of the gamma photons emitted by a scintillation camera or gamma camera provides a representation of the spatial distribution of radioactivity (Tab.1).

The main benefit of the test

It lies in the early onset and intensity of the metabolic changes detectable by BS, often several weeks before any radiological image appears. It also lies in the fact that the examination explores the entire skeleton at a relatively modest dosimetric cost.

The benefits of SPECT/CT complementation

This functional imaging technique enables topographical diagnosis, quantification and monitoring of bone lesions. It is a reproducible and highly sensitive examination that enables the entire skeleton to be analysed in a single session. However, the specificity of planar BS remains poor for diagnosing (Tab.2) certain areas of radiotracer hyperuptake, particularly in the axial skeleton. BS may show hyperfixation in the case of osteocondensing lesions or hypofixation in the case of pure lytic lesions with no oedematous reaction. Normofixation is reassuring in principle, but may also correspond to small lesions. Spinal, pelvic and cranial locations are better analysed by hybrid SPECT/CT imaging, which allows precise anatomical location of lesions and improved specificity, helping to reduce the proportion of indeterminate BS results (from 60 to 70%) and reducing the need for further radiological investigations. In fact, numerous studies have demonstrated the diagnostic benefit of SPECT/CT compared with SPECT alone and planar scintigraphy for characterising bone lesions in the combination of rheumatological and oncological indications when these lesions are undetermined (5).

Methods of bone scintigraphy

- Physical characteristics of the radionuclide: Tc99m has a half-life of 6 hours and decays by isomeric transition into technetium 99, emitting gamma radiation with a characteristic energy of 140 keV, which makes it easy to detect. Technetium 99m is industrially produced by the molybdenum 99 isotope in molybdenum/technetium generators at nuclear reactors (6).

- Characteristics of the vector molecules used: The carrier molecule belongs to the family of Bisphosphonates, characterised by a P-C-P chain.
Depending on the possible substitutions on the central carbon atom, there are several molecules that can be used in bone scintigraphy:

- MDP (Methylene Di Phosphonate),
- EHDP (Ethylene Hydroxy Di Phosphonate),
- HMDP (Hydroxy Methylene Di Phosphonate),
- DPD (Dicarboxy Propane Diphosphonate).

Available as radiolabelled single doses from radiopharmaceutical distributors or as commercial radiolabelling kits. The kits are supplied in a vial containing the bisphosphonate, a stannous reducing agent and other excipients in powder form, ready for labelling (7).

- **Pharmacokinetics:**
  After intravenous administration, technetium oxidronate (99mTc) is rapidly distributed into the extra-cellular space. Plasma clearance of DP is bi-exponential: linked to bone uptake and urinary elimination of the radiopharmaceutical. Bone uptake is almost immediate and progresses rapidly, 30 minutes after injection, 10% of the injected activity is still present in the bloodstream. This value decreases to 5%, 3%, 1,5% and 1% respectively within 1, 2, 3 and 4 hours after injection.

4 hours after injection:
- 60% of the quantity injected is fixed on the skeleton,
- 34% is eliminated in the urine,
- 6% remains in circulation.

Elimination occurs via the urine: approximately 30% of the administered activity is eliminated within the first hour, 48% within 2 hours and 60% within 6 hours (8).

- **Fastening mechanisms:**
  The injected DP are adsorbed onto the surface of the hydroxyapatite crystals, depending on blood flow and local osteoblastic activity.

- **Preparation of the radiotracer:**
  Vials containing sterile, pyrogen-free lyophilisate are ready for 99mTc labelling. Preparation is carried out in accordance with the manufacturer’s recommendations (4).

- **Shelf life:**
  Estimated at 1 year; 8 hours after marking for the product marked at laboratory temperature (4, 8).

- **Special storage precautions:**
  The kit and the marked product should be stored in a refrigerator (between 2°C and 8°C) and used until the expiry date of the batch.

Radiopharmaceuticals must be stored in accordance with national regulations relating to radioactive products (8).

- **Scintigraphic examination:**
  - Information required for a quality review:
    1. Reason for examination
    2. History of bone or joint pathology
    3. Symptoms and clinical data (bone pain +++)
    4. Results of laboratory tests and any imaging tests (X-rays, CT scan, MRI, previous BS)
    5. Treatment likely to alter scintigraphy results (anti-inflammatory drugs, antibiotics chemotherapy, radiotherapy)
    6. History of kidney or urinary tract disease

- **The patient:**
  - No special preparation of the patient, apart from the usual precautions applied for any irradiating examination, in women during the period of genital activity.
  - There’s no need for fasting.
  - Good hydration (1.5 to 2.5 litres of water ½ h after the injection so as not to reduce the fixation of the tracer on the skeleton)
  - Emptying the bladder immediately before taking late images, hyperdiuresis will accelerate the elimination of circulating activity, improving the signal-to-noise ratio and reducing bladder and peri-bladder irradiation, particularly in the ovaries.

- **Injected activity:**
  - Peripheral IV injection, outside the site of interest, under the gamma camera if the early protocol is indicated:
    a) 5- 20 Mci or 555 - 740 MBq for a weight of 70 kg,
    b) In children 8 MBq / Kg with a minimum dose of 20 MBq (3).
  It should be noted that in certain special cases (obesity, extreme thinness), the injected activity may exceed the recommended limits, but it should remain as close as possible to the recommended limits.
  The scan speed and the time between injection and acquisition can also be adjusted to optimize images.

- **Acquisition:**
  Multiple-phase BS has been performed for many years, initially on localised osteoarticular or musculoskeletal lesions, in order to increase the reliability of BS. Multi-phase BS was initially used to detect osteomyelitis, particularly in children, inflammatory joint and bone pathologies, post-operative status and acute fractures.
It is now possible, with all the multi-detector gamma cameras available on the market, to easily obtain bone scintigraphy three-phase pan-corporeal (BS3PP). Obtaining BS3PP can be useful in pathologies potentially affecting more than one bone or joint, helping to improve the reliability of SO and its ability to characterise lesions (1).

- **Examination protocol:**
  - Angiographic time: immediate recording of a series of images representing the arrival of the tracer in the pathological region to be explored.
  - Tissue time: static images of the regions to be explored during the tracer diffusion phase in the tissue, acquired between 0 and 10 minutes after injection of the tracer when it has not yet attached itself significantly to the bone (Tab.3).
  - Bone time: images after 2 to 4 hours post-injection (later in cases of renal failure or micturition disorders), whole body scan +/- tomography

**Bone tomoscintigraphy:**
- Pinpoints the location of abnormal images and boosts contrast.
- Matrices of 64 x 64 x 16 or more.
- Consists of 64 or more images, recorded in a circular or elliptical orbit of 360°patients in decubitus or 180°patients in procubitus for analysis of the spine, each image lasting between 10 and 40 seconds.
- A pinhole collimator:
  - High resolution, for small areas (infants) acquisition involves 50 to 100,000 shots per image.
  - Localized acquisition under various impacts:
    - Useful for specifying topography, extension and helping to diagnose the nature of abnormal images.
    - Frontal, profile, oblique, special, flexion, extension and rotation incidences can be performed on various joints.
    - Multiple incidences, particularly oblique or caudal, over the pelvis when bladder activity impedes visualisation, views can be repeated later, immediately after making the patient urinate again, in some cases, after urinary catheterisation.

- **Image processing:**
  - Planar images do not require any special processing. It should be noted that careful viewing of the digital images acquired by today’s computerised cameras enables the full range of contrasts to be explored and greatly improves the diagnostic value of the examination. A linear grey-scale contrast scale is used, with reproduction on film (after or without digitisation) or on paper in video mode.

- The tomographic images must be processed, and the images reconstructed using filtered back-projection or, better still, an iterative method.

- **Scintigraphic semiology:**
  a) **Normal scintigraphy:**
    - The interpretation of a bone scan is based on the fundamental principle of symmetry, with a comparative study of the bone parts.
    - In adults, the images show areas of more marked fixation due to their metabolic activity, their thickness or their close proximity to the detection system.
    - On the anterior surface: facial mass, sternum, humeral heads, anterior costal arches and iliac crests.
    - On the posterior surface: the tips of the shoulder blades, the posterior costal arches, the spine and the sacroiliac joints.
    - In children and adolescents, bone scintigraphy is characterised by hyperactivity of the fertile metaphyses, in particular the upper ends of the humeri and tibias, the lower ends of the femurs, and to a lesser extent the ankles and wrists.
    - In the elderly, fixation is generally reduced due to physiological osteopenia.

  b) **Anomalies and interpretation:**
    Two fixation abnormalities have been described: hyperfixation and hypofixation.
    - Hyperfixation is the most frequent abnormality and is characterised by:
      1. Intensity: very intense, moderate or low.
      2. Homogeneity or heterogeneity.
      3. Appearance, shape and clear or irregular boundaries.

    BS is a sensitive but (Tab.2) non-specific test, with many pathologies producing hyperfixations that do not allow the aetiology to be determined.
- A single scintigraphic anomaly is always difficult to interpret, and must be taken into account in the clinical and radiological context.
- The scintigraphic images regress over long periods, reflecting the slowness of the bone remodelling process, which takes place over several months. It is therefore usually unnecessary to repeat the scintigraphic examination before 4 to 6 months.

c) Artifacts and sources of error:
- Radiation attenuated by metal parts or patient movement.
- Extravasation of RP during intravenous injection.
- Radioactivity of urine, in cases of dilatation, stasis or malposition of the urinary tract, particularly after urological surgery, or contamination during urination.
- Soft tissue hyperfixation may occur in cases of myositis ossificans, calcified haematoma, tissue necrosis or tumour necrosis.
- Some bone tumours may be purely lytic and not very visible on scintigraphy when they are small (certain myelomas or certain metastases, particularly of renal origin).

Dosimetry:
The dose delivered to the body for a bone scan is of the order of mGy, and is often considered to be equal to 1/10th of the dose delivered by a standard radiological examination and one hundredth of that delivered by an IVU.
- Whole body: 2.7 mGy / MBq
- Skeleton: 11.1 to 12.5 mGy / MBq BM: 5.4 to 8.9 mGy / MBq
- Bladder: 37 mGy / MBq Ovaries: 3.5 mGy / MBq

Conduct of the examination in the Nuclear Medicine Department of the HASSAN II University Hospital in Fez:
In the first few minutes (0-10 min) following intravenous injection of the radiopharma-ceutical, a so-called «early» image is produced. At this stage, contrast depends on local vascularisation: areas of bone remodelling appear hypervascularised. Some soft tissue infections may be visible at this stage. This is followed by a delay of at least 1.5 hours to allow the radiopharmaceutical to bind to the bone tissue. The patient is therefore encouraged to drink to quickly eliminate the urinary activity. After the incompressible fixation time, the images, known as «bone time» are taken. For children, ideally the parents should always be present to ensure that the child does not sleep, so that the child can have a nap during the examination. The presence of the parents, gentle restraint, the kindness of the manipulators and the use of distractions such as a DVD player make it easier to take the images. The entire skeleton is examined, which is invaluable in cases where the location of the pain is imprecise: infants, disabled children, etc. This is done either by scanning the skeleton over a period of 20 minutes, or in the case of the youngest patients, by localised images, each lasting 5 minutes. This procedure can be interrupted and repeated as often as necessary, with no impact on the radiation dose received, to obtain clear images, with the possibility of pauses between two images. These planar images are supplemented if necessary by tomographic acquisitions, if the child is calm, or images enlarged using the pinhole collimator.

Examples of bone scintigraphic examinations obtained in three pan-corporeal phases carried out in the Nuclear Medicine Department of the HASSAN II University Hospital in Fez:

Clinical case N°1
Septic Pseudarthrosis:
29-year-old female patient, followed for a post-traumatic comminuted fracture of the left femur, initially treated for osteosynthesis with a screw plate removed after a local infection, followed by an external fixator.
TAP scan: Consolidation of the fracture site on the left femoral shaft still ongoing, slightly more advanced than on the previous scan, with no evidence of an intraosseous or soft tissue abscess. Bone scan ordered on suspicion of septic pseudarthrosis: In the early stages hyperhaemetic focus at tissue and vascular time opposite the upper-middle third junction of the left femoral diaphysis (Figure a). At late stage and additional SPECT CT: A focus of bone hyperfixation involving the femoral shaft opposite the junction of the upper third and middle third of the left femoral shaft, related to an infection. Heterogeneity of the fixation in relation to the left femoral shaft, related to the ongoing consolidation process. A focus of hyperfixation opposite the 1st plug of the upper end of the external fixator, related to a reactive osteoblastic reaction (Fig.1). Scintigraphic appearance suggestive of septic pseudarthrosis with individualization of an infectious focus opposite the junction of the upper third and middle third of the left femoral shaft.
Clinical case N°2
Primary osteochondritis:
10-year-old child with apyretic left-sided limp for one year. CT scan of the pelvis: showing an osteolytic image of the left acetabulum opposite the coxofemoral joint with infiltration of the soft tissues and a small amount of joint effusion related to an infection or tumour.

A bone scan was ordered to establish the diagnosis. Early stage showing no asymmetry in perfusion or tissue uptake of the osteotropic radiotracer in the coxofemoral projection (Fig. 2 a). Pinhole: intense, linear hyperfixation opposite the epiphysis of the left femoral head, which appears to have lost its sphericity, extending towards the epiphyseal core (Fig. 2 b). Whole body: Strengthening of left acetabular and trochanteric fixation with a reaction-like appearance and fairly homogeneous and symmetrical distribution of the radio-pharmaceutical over the rest of the skeleton (Fig. 2 c). Scintigraphic appearance suggestive of Primary Osteochondritis at stage IIIB of Conway’s classification.

Clinical case N°3
Multiple brown tumours:
46-year-old patient on chronic haemodialysis with hyperparathionemia at 10fold above normal
levels. The diagnostic CT scan: showed osteolytic lesions involving the right sacral fin and the left 6th rib, including the right sacral fin with epidural and sacral foramen extension. Bone scan: In the early stages: frank hyperaemia in the right sacral projection. Late period: Large focus of very intense hyperfixation opposite the sacrum in relation to the locating CT sections with a lytic lesion involving the entire right sacral fin with lysis of the cortical bone (Fig. 3 b + d). Focus of hyperfixation in the middle arch of the 6th left rib corresponding to a blowing lytic lesion (Fig. 3 b + c). Discrete hyperactive focus of the distal end of the right femur corresponding to an enchondroma (Fig. 3 b + e). Bone scintigraphy combined with SPECT-CT revealed multiple brown tumours, particularly over the 6th left rib and the right sacral fin, given the patient’s clinical context. Management was completed by a bone biopsy which showed an immature bone regenerative reaction with no tumour lesion within the limits of the cores examined.

**Clinical case N°4**

**Osteoblastoma:**

11-year-old boy presenting with pelvic pain without lameness and painless palpation and mobilisation on clinical examination. Bone scintigraphy: Early stage: Tissue hyperuptake of radiotracer in the left hip (Fig. 4 a) Late stage:
Intense hyperfixation of the bone opposite the left ischiopubic ramus, corresponding to a well-limited osteolytic blowing lesion surrounded by peripheral osteocondensation with local cortical rupture (Fig. 4a + b). In addition, there was no clearly identifiable bone fixation anomaly on the rest of the skeleton explored. Bone scintigraphy combined with SPECT-CT revealed osteoblastoma.

Clinical case N°5
Active neurogenic para-osteoarthropathy:
A 10-year-old child with a history of hospitalization in intensive care for management of a polytrauma, whose evolution was marked by the development of a neurogenic para-osteoarthropatic syndrome involving both hips and the right knee. Bone scintigraphy: Early stage: Accumulation of radiotracer in the right hip, knee and ankle (Fig. 5a). Late stage: Hyperfixation of both hips, right knee and ankle. There were no clearly identifiable bone fixation abnormalities on the rest of the skeleton explored (Fig. 5b). The scintigraphic configuration of the two right hips, knee and ankle is in favour of an active neurogenic para-osteoarthropathy.

Clinical case N°6
Unifocal Langerhansian histiocytosis:
A 15-year-old adolescent presented with left hip pain. X-rays of the pelvis and MRI of the hip revealed a geodic lacunar image of the left greater trochanter, followed by a benign tumour lesion of the left greater trochanter with a peri-lesional inflammatory reaction. Bone scan: in the early stages: discrete hyperaemia over the left hip. Late stage: asymmetric bone fixation in relation to both hips at the expense of the left side, complemented by SPECT-CT scans which reveal the bony lesion of the left greater trochanter described on the X-ray, which is a lacunar lesion with blurred contours and no hypertrophy of the soft tissues in relation to it. Bone scintigraphy coupled with SPECT-CT revealed that the bone lesion described oppo-
site the left greater trochanter on morphological examinations was probably in favour of unifo
cal Langerhansian histiocytosis (Fig. 6 a - c). After undergoing a bone biopsy following a bone scan, the suspected diagnosis was confirmed through histological and immuno-histochemical examinations.

Clinical case N°7
Osteogenesis Imperfecta Type IV:
Patient aged 40, of short stature, with a history of spontaneous fracture of the right femur. Fibrous dysplasia of the right arm is suspected.

At the late stage: linear hyper-fixation opposite the upper third of the left femur in relation to the patient’s history of trauma (Fig. 7 a). In addition, there are a number of objective deformations: an arcuate curvature of the long bones of the upper and lower limbs, with local thinning of the cortical bone (Fig. 7 b). A heterogeneous, enlarged appearance of the sternum (Fig. 7 d). Straightness of the spine (Fig. 7 c). Bilateral renal lithiasis (Fig. 7 e). Scintigraphic appearance primarily suggestive of osteogenesis imperfecta type IV according to the Silence and Glorieux classification.

Clinical case N°8
Unifocal osteoarthritis:
Suspicion of polyarthritis in a 9-year-old boy with a history of septic arthritis of the ankles and hip who underwent surgical drainage. Presently has a painful swelling of the left ankle with fever. Bone scan: in the early stage asymmetry in radiotracer uptake and perfusion in relation to the two ankles, more marked on the left. In the late period: a strengthening of the bone fixation around the left ankle. On the rest
of the skeleton, there was no clearly identifiable bone fixation anomaly (Fig. 8). Scintigraphy in favour of unifocal osteoarthritis of the left ankle.

**Clinical case N°9**

**Polyostotic Fibrous Bone Dysplasia:**
Suspicion of fibrous dysplasia in a 46-year-old patient. TAP scan: Multiple lytic lesions of the axial and peripheral skeleton with a benign appearance, possibly related to polyostotic fibrous dysplasia or multiple enchondromatosis. The scintigraphic examination showed diffuse heterogeneity of bone fixation, particularly opposite the implant (Fig. 9); and also of the anterior arch of the left K7 and the anterior and middle arch of the right K9. The sacrum and iliac bones, of the left iliopubic and ischiopubic branches, both femurs and both tibias Scintigraphic appearance in favour of polyostotic fibrous bone dysplasia.

**Clinical case N°10**

**Paget's disease:**
A 75-year-old patient with a Gleason score of 7 (4+3) and PSA = 17.25 ng/ml for prostate adenocarcinoma. A bone scan was ordered as part of an extension assessment, which revealed intense, homogeneous bone hyperfixation, particularly in the following areas: (Fig. 10) of the left hemipelvis, from the upper half of the right femur, from the whole of the left femur. Scintigraphic appearance suggestive of Paget's disease. The examination was completed by an alkaline phosphatase assay, which was found to be elevated.

**Clinical case N°11**

**Osteonecrosis of the right femoral head:**
15-year-old child admitted for management of right hip dislocation with suspected necrosis of the right femoral head. The TAP scan performed 4 months before the bone scan was unremarkable. Bone scan: In the early stages: asymmetry of radiotracer uptake and perfusion in favour of the right hip (Fig. 11 a). In the late phase: bone hyperfixation over the entire right femoral head with discrete heterodensity as seen on the locating CT scan (Fig. 11 b). Scinti-
graphic appearance in favour of osteonecrosis of the right femoral head (Stage III).

**Clinical case N°12**

**Osteoid Osteoma:**

15-year-old girl with chronic right ankle pain for two years. Bone scan ordered to explore the ankle and showing: in the early stages: moderately intense hyperhaemia on the outside of the right ankle. In the late stages: asymmetry of bone fixation between the ankles in favour of the right side, with individualisation of a focus of hyperactivity projecting from the lateral malleolus. Complementary SPECT CT reveals a lacunar bone lesion with cortical thickening and nidus, suggesting (Fig. 12) an osteoid osteoma.

Scano-scintigraphic appearance suggestive of osteoid osteoma of the lateral malleolus of the right ankle.

**Clinical case N°13**

**Active Hypercondylism:**

Suspicion of left hypercondylism in a 43-year-old patient. Bone scan: Early stage: Absence of asymmetry of uptake and perfusion in the two condylar regions (Fig. 13 a). Late: Discrete asymmetry of bone fixation in relation to the two condyles, more marked on the left. Complementary SPECT-CT reveals clear hyperfixation opposite the left condylar process with bone hypertrophy, suggesting an active disease process (Fig. 13 b). Scano-scintigraphic appearance in favour of active hypercondylism.

**Clinical case N°14**

**Renal Osteodystrophy:**

A 48-year-old chronic haemodialysis patient presented with spinal pain for 8 months, aggravated by walking difficulties, all in an apyretic setting. A spinal MRI revealed multiple osteoporotic settlements. Bone scintigraphy showed intense and relatively homogeneous hyperfixation over the entire skeleton, more marked over the skull and facial bones, and increased...
fixation along the long bones, with no visualization of the urinary tract, suggesting a metabolic superscan. Focal hyperfixation of the posterior arch of the 11th left rib and the proximal end of the femurs, which may suggest bone fissures. The spinal axis shows multiple images of intense, homogeneous hyperfixation, more marked in the lumbar spine, suggestive of multiple osteoporotic settlements. The scintigraphic appearance is suggestive of renal osteodystrophy (Fig. 14).

**Conclusion**

In daily routine, the diagnostic process begins with clinicians identifying pertinent clinical factors and areas of uncertainty, resulting in a preliminary diagnosis. Nuclear physicians then customize the scintigraphic examination to address specific clinical concerns. It is crucial to recognize that the clinical cases provided here are illustrative examples, and not absolute standards for image quality or equipment configurations. Our cases are designed to prompt individual reflection, tailored to the nuances of each individual clinical scenario.

**Conflict of interest:**

The authors declare that there were no conflicts of interest within the meaning of the recommendations of the International Committee of Medical Journal Editors when the article was written.

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