

## ROLE DE LA MEDECINE NUCLEAIRE

### 1. Quelle est la place de la scintigraphie osseuse aux biphosphonates ?

#### 1.1 Quelles sont les performances de la scintigraphie osseuse ?

La scintigraphie osseuse aux biphosphonates, est une méthode pour explorer l'ensemble du squelette. Elle est largement disponible et induit une faible irradiation (4 mSv environ). Elle détecte les métastases osseuses plus précocement que les radiographies conventionnelles (2-18 mois avant). Dans la littérature, sa sensibilité et sa spécificité sont appréciées de façon variable selon les études (sensibilité 62-100% ; spécificité 61-100%). Classiquement, on considère que sa sensibilité est bonne surtout pour les métastases ostéocondensantes, mais que sa spécificité est médiocre pour le diagnostic des métastases osseuses ostéolytiques. La bonne sensibilité est expliquée par le fait qu'une métastase impliquant seulement 5% de la pièce osseuse suffit pour être détectable.

L'utilisation complémentaire de la SPECT-TDM (tomoscintigraphie couplée à un scanner low dose) améliore les performances de l'examen (sensibilité 98%, spécificité 81%) en permettant une excellente localisation. Cependant il faut noter qu'elle n'est réalisée que pour affiner l'analyse d'une lésion suspecte sur le balayage.

Les faux négatifs de la scintigraphie osseuse (10-20% selon les séries) sont essentiellement liés à des lésions ostéolytiques très agressives sans réaction ostéoblastique associée, comme c'est le cas après une radiothérapie et pour des cancers broncho-pulmonaires, du rein ou de la thyroïde. **Figure 2.**

La scintigraphie osseuse dans le cadre de bilan d'extension du cancer broncho-pulmonaire n'est pas indiquée si une TEP-FDG a déjà été réalisée car elle est moins performante.

Le lecteur trouvera les détails dans les références annexées (28-33).

#### 1.2 Qu'appelle-t-on « flare up » ?

L'intensité de la fixation aux temps tardifs est corrélée avec le degré d'évolutivité des lésions, mais **pour certaines lésions initialement très lytiques, on peut au contraire assister, alors que le traitement oncologique est efficace, à une augmentation de la fixation due à la reconstruction osseuse concomitante (forte activité ostéoblastique) suite à la disparition du tissu tumoral** et même de l'apparition de nouveaux foyers de fixation. Comme les critères d'évolution reposent sur l'intensité et surtout sur le nombre de foyers hyperfixants, lors de l'évaluation de deux scintigraphies successives sous traitement, **une attention particulière devra être portée à la réponse globale (état général du patient, extension tissu mou et os) et à la chronologie pour ne pas rater un "flare up phenomenon"** (34). La visualisation des foyers d'hyperfixation apparemment supplémentaires correspond en réalité à des lésions préexistantes passées inaperçues en raison de l'absence de réaction ostéoblastique (28,31).

Le *flare* a été décrit pour des métastases osseuses provenant de tumeurs malignes très diverses (poumon, prostate, sein, ostéosarcome, lymphome). Cette accentuation des hyperfixations concerneait entre 15 et 30 % des patients. Les patients dont la scintigraphie osseuse montre un *flare* ont un pronostic analogue à ceux dont la scintigraphie objective une amélioration sans *flare* (28).

**Pour le clinicien, le *flare-up* est un piège diagnostique et ne doit pas être assimilé à une progression métastatique faisant modifier le traitement de façon intempestive.** Programmer la scintigraphie osseuse de contrôle après le sixième mois permet d'éviter ces difficultés d'interprétation car au-delà de ce délai, une accentuation des foyers préexistants, ou une apparition de nouveaux foyers sur la scintigraphie osseuse signent une progression métastatique (28). Si la scintigraphie osseuse précoce s'avère nécessaire (moins de 6 mois), la distinction entre *flare* et progression métastatique repose sur un faisceau d'arguments : l'état clinique (amélioration ou détérioration de l'état général), l'aspect des radiographies standards (recalcification ou aggravation de l'ostéolyse), des éventuels marqueurs tumoraux et la cinétique comparative des marqueurs

osseux (phosphatases alcalines osseuses pour l'ostéoformation et extrémité C-terminal du collagène de type I pour l'ostéorésorption). Il est parfois nécessaire de recourir à l'IRM, qui montre une disparition de l'infiltration métastatique ostéomédullaire en cas de *flare*.

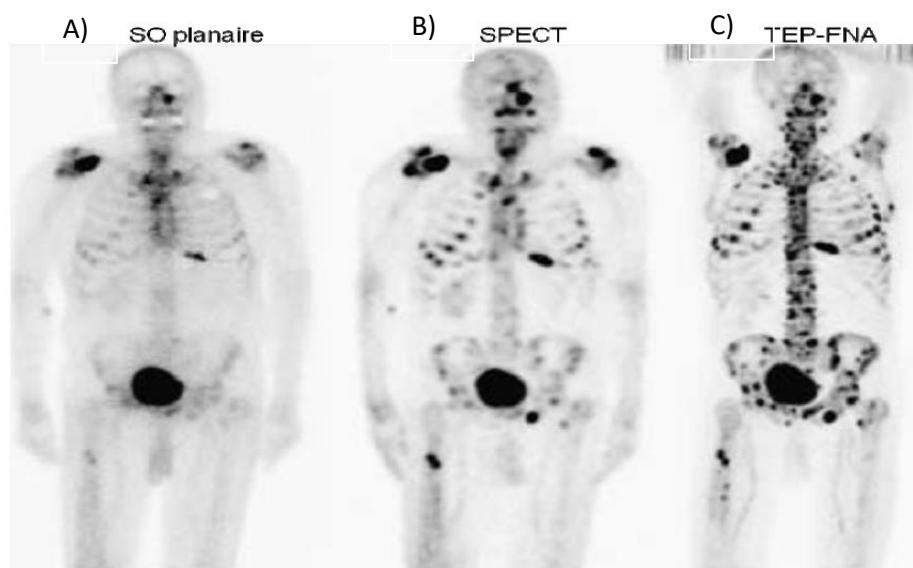
Dans tous les cas, en l'absence de nouvelle douleur osseuse, la réalisation d'une scintigraphie osseuse systématique au cours du suivi ne semble pas indiquée.

## 2. Quelle est la place de la scintigraphie TEP-FDG ?

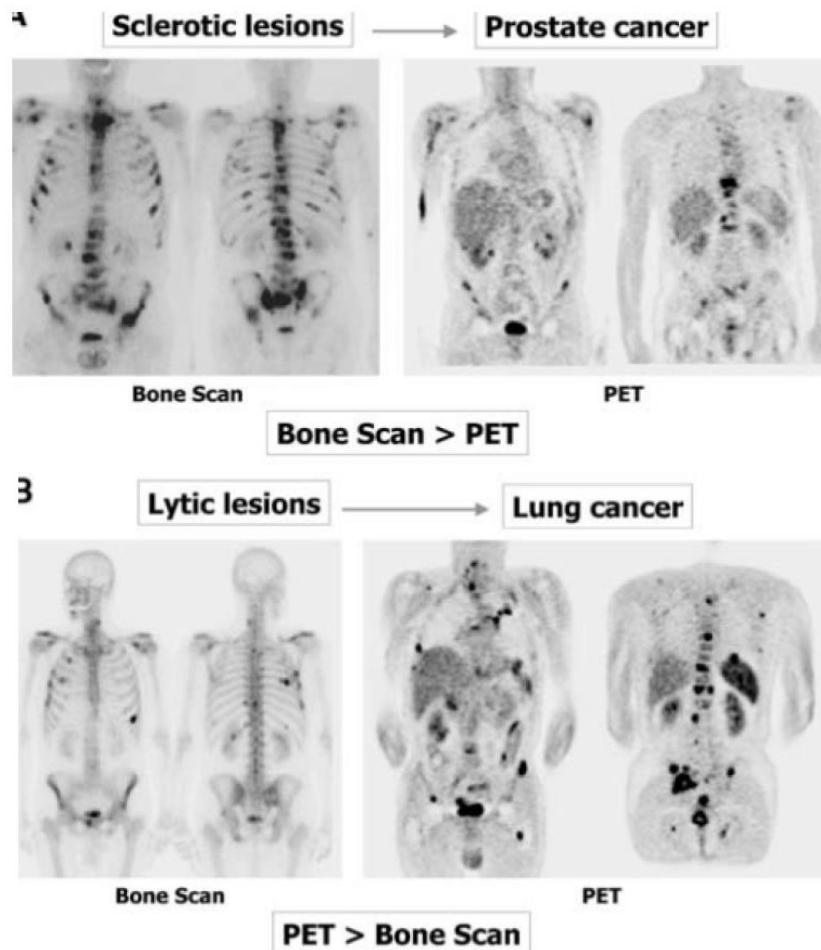
L'utilisation du fluoro-déoxyglucose marqué (18FDG) repositionne la démarche diagnostique et thérapeutique dans de nombreux domaines de la cancérologie. L'avidité des métastases ostéolytiques pour le 18FDG est supérieure à celle des métastases ostéocondensantes, c'est pourquoi la sensibilité de la scintigraphie au 18FDG apparaît plus élevée dans les cancers mammaires, coliques ou bronchiques, que dans le cancer de la prostate (surtout si le score de Gleason n'est pas élevé). **Figure 3.** Plusieurs facteurs ont été incriminés pour rendre compte de cette différence de sensibilité : cellularité tumorale plus faible en cas de métastases condensantes, hypoxie cellulaire en cas de métastases lytiques, influence de l'hormonothérapie... L'examen peut être contributif dans la recherche d'une maladie occulte ou pour caractériser une anomalie douteuse en scintigraphie du squelette. **La TEP-FDG est soumise à la même problématique de flare-up que la scintigraphie osseuse car l'activité ostéoblastique est fortement consommatrice d'énergie.**

## 3. Quelle est la place de la scintigraphie osseuse TEP-18FNa ?

Le 18F-Na possède un tropisme osseux obéissant à un mécanisme similaire aux radiobisphosphonates et procure des images très fines avec une résolution supérieure à celle de la scintigraphie osseuse. Ce gain de résolution spatiale provient notamment des propriétés pharmacologiques du 18F-Na (captation osseuse 2 fois plus élevée et clairance sanguine plus rapide que les bisphosphonates) et de la technique de détection TEP. Les propriétés des caméras TEP et du 18F-Na aboutissent à une sensibilité et une spécificité de la technique supérieures à la scintigraphie osseuse, même complétée par une tomoscintigraphie (31). Elle est encore peu disponible.



**Figure 2 - Comparaison pour un même malade des résultats d'une scintigraphie osseuse (A), d'un PET-scan au FDG (B) et d'un TEP-NAF (C) dans un adénocarcinome pulmonaire. Les lésions sont très ostéolytiques et mal identifiées en scintigraphie osseuse planaire par rapport au TEP-FDG (B) et au TEP-NAF (Extrait de Even-Sapir et al., JNM, 2006).**



**Figure 3 - Scintigraphie osseuse aux BP-(99mTc) vs TEP au FDG-(18F). La sensibilité lésionnelle dépend du phénotype (condensant ou lytique) des métastases osseuses (Extrait de Even-Sapir et al., JNM, 2006).**

## Recommendations

- La scintigraphie osseuse est moins sensible que la TEP-FDG pour le bilan d'extension des cancers broncho-pulmonaires (sous-estimation des lésions très ostéolytiques).
  - En dehors d'une question clinique précise, la scintigraphie osseuse n'est pas indiquée pour le suivi.
  - Le TEP-FDG représente un bon examen pour cartographier les métastases osseuses ostéolytiques du cancer du poumon sous réserve de réaliser un balayage suffisamment étendu (incluant au moins les fémurs).
  - Une lésion isolée en TEP ou en scintigraphie osseuse : doit faire réaliser une imagerie ciblée suivie d'un avis spécialisé (fréquence des diagnostics différentiels).
  - L'interprétation d'une imagerie métabolique précoce doit prendre en compte la possibilité du *flare*. Une interprétation dans l'ensemble du contexte (clinique et paraclinique) est nécessaire.



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