

## Serum C-terminal telopeptide (CTX) A new test for monitoring bone health

### What is CTX?

CTX is a bone turnover marker (BTM) for monitoring osteoporosis drugs such as denosumab or the bisphosphonates. On a biochemical level, it is the polypeptide chain linking the three strands of type I collagen at their C-terminus. The CTX test was developed in the mid-90's<sup>1</sup> and since that time has become the most commonly used serum- or urine-based biomarker for osteoporosis research and clinical drug trials.

### What are the applications of this test?

- Monitoring osteoporosis patients for compliance with treatment and identifying the presence of medical conditions that diminish the effectiveness of drug therapy.

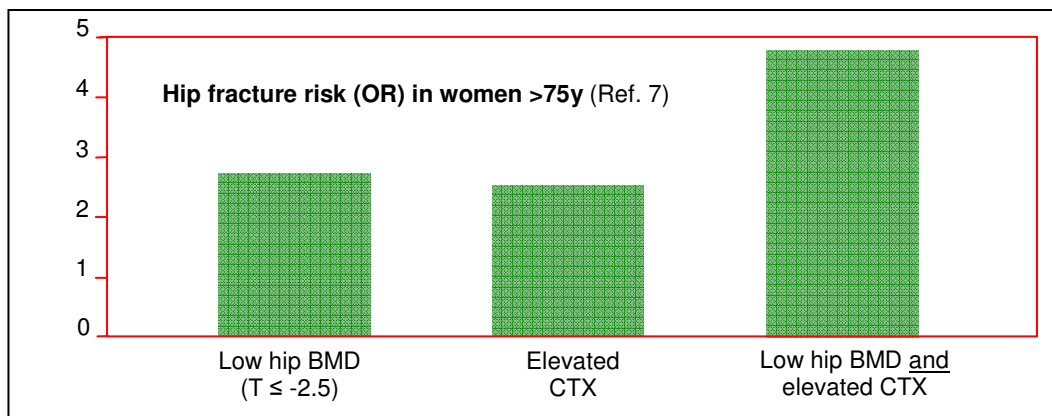
Compliance rates for bisphosphonates in general practice are very poor, with 50-75% of patients discontinuing therapy within the first year<sup>2,3</sup> and experiencing a significantly increased fracture risk (45% in one study<sup>4</sup>). A CTX test can not only enhance patient motivation<sup>5</sup> to adhere to therapy but provide objective evidence of a patient's compliance with orally administered medication.

DEXA also offers this information but it will not be available to the physician for nearly two years due to bone's slow rate of microarchitectural change. CTX, by contrast, can provide the answers within weeks.

- An independent predictor of fracture risk.

Current BC guidelines for DEXA testing severely restrict its use for a patient <65y who is concerned about their risk of a non-traumatic (*i.e.* potentially preventable) fracture. In the absence of co-morbidities or a previous fracture, such a patient is unable to properly inform themselves about their likely risk. The absence of a BMD measurement, in turn, diminishes the value of risk prediction tools such as FRAX<sup>®6</sup>. It is this vacant diagnostic space which the CTX test is intended to occupy. Note that BTM's are not included in FRAX<sup>®</sup> because of insufficient data rather than a clear demonstration of no added value.

It is important to realize that CTX does not replace DEXA or any other diagnostic tool. Rather, it is meant to provide complementary information about the entire skeleton, as indicated by the graph below:



### What is the value of measuring CTX to monitor response to bisphosphonates when the clinical trials literature shows such a consistent effect?

Cohorts from the clinical trials literature differ markedly from patients seen in regular practice, making the transferability of the studies' conclusions questionable. One osteoporosis clinic<sup>8</sup> found that the vast majority (80-97%) of its new patients, diagnosed with osteoporosis, would not have been eligible for one of its clinical trials, mainly on the grounds of co-morbidities, age and disease severity. Moreover, the >80% compliance rates in such trials greatly exceed those encountered by the general practitioner.

## How is LifeLabs serum CTX better than existing bone marker tests?

The serum CTX test provides a more reliable assessment of overall bone resorption by overcoming the limitations of the current urine deoxypyridinoline cross links test, such as high within-patient variability and unreliability in the presence of renal impairment<sup>9</sup>. Moreover, having this MSP-unlisted test performed locally at LifeLabs provides significant savings to the patient.

## Many patients with newly-diagnosed osteoporosis present with a recent fracture. How will this affect the utility of CTX?

Serum CTX will be elevated for one year following a fracture. However, levels will not rise significantly within 1 day of the fracture<sup>10</sup>. A blood sample collected within this period could still be used to establish a baseline for subsequent investigations.

## What is the value of measuring CTX for BRONJ risk?

Serum CTX has been promoted by some<sup>11,12</sup> but not all<sup>13,14</sup> dental surgeons as a risk marker for bisphosphonate-related osteonecrosis of the jaws (BRONJ). There is no official position on this matter by either Canadian or American dental associations. The test is not intended to unambiguously identify patients who will acquire BRONJ following oral surgery: rather, CTX <0.15 ng/mL in a patient on bisphosphonate therapy (especially intravenous) is associated with an increased risk of BRONJ. In such cases, it has been suggested that the drug be discontinued prior to surgery<sup>15</sup>.

## Can CTX be used to evaluate the risk of subtrochanteric fracture?

No; while there is good evidence from histomorphometric and tetracycline labeling studies suggesting excessive suppression of bone turnover in such fractures, BTM results have been unable to support these findings<sup>16,17</sup>. However, this is almost certainly due to samples having been collected well after the initial fracture at a time when bone turnover was increased (see above).

## Biological and analytical variation have been said to limit the usefulness of bone turnover markers. How has LifeLabs addressed these issues?

All samples are collected under standardized conditions (e.g. fasting, AM, avoidance of strenuous exercise, stable diet). For a given patient, the baseline sample is stored until the follow-up sample is collected at 3 months, whereupon both are processed together in a single batch. This feature eliminates the inherent between-run variability of tests such as urine cross-links and differentiates LifeLabs CTX test from those offered elsewhere.

## References

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