

# Does karyotyping and in situ hybridization from three different germ layers elucidate low bone mineral density in Turner syndrome?

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## Objective:

The aim of this study was to elucidate whether karyotype differs among the tissues originating from the three different germ layers and whether this is associated with bone mineral density (BMD) in girls with Turner syndrome (TS).

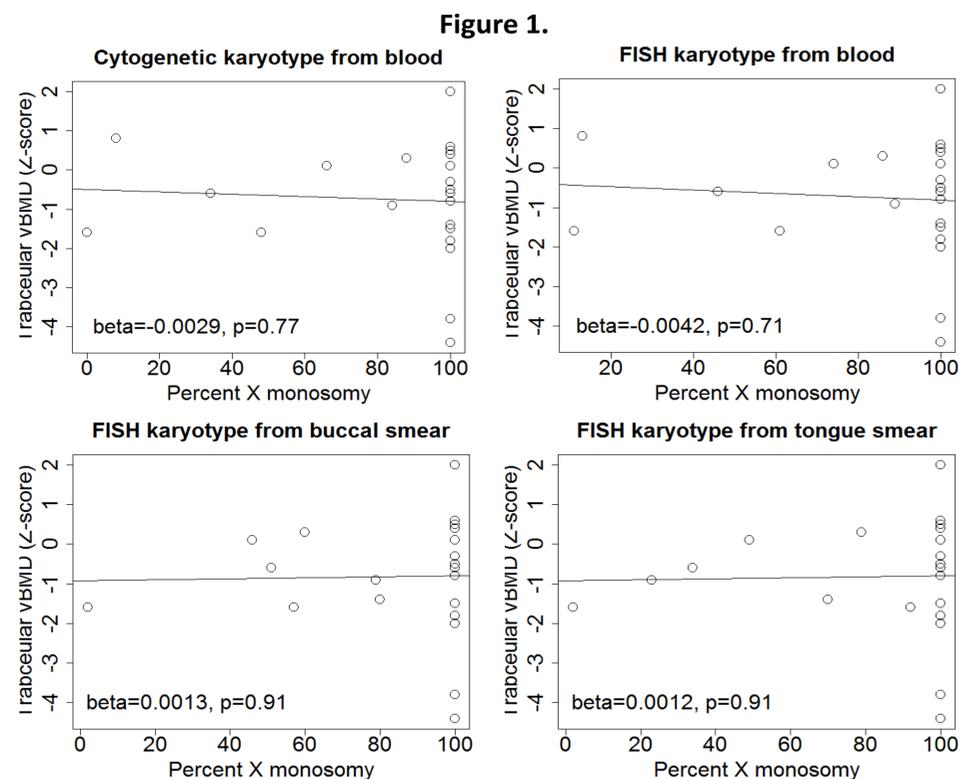
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## Background:

Turner syndrome (TS) is caused by a total or partial loss of one X chromosome. **Trabecular BMD decrease and total bone cross-sectional area increase during puberty** has been reported at the radius by peripheral quantitative computerized tomography (pQCT). **Chromosomal aberration is considered one of the probable causes of bone changes in TS.**

**Table 1.** Anthropometric characteristics of girls with TS.

(N=29)	Mean (SD)	Median (min; max)
Age [year]	12.6 (3.7)	11.8 (6.0; 18.3)
Height [Z-score]	-1.7 (0.9)	-1.8 (-3.5; 0.6)
BMI [Z-score]	0.3 (0.9)	0.2 (-1.8; 2.2)
Tanner Breast Dev. St. [1-5]	15/3/0/2/9	
Postmenarcheal [yes/no]	9/20	



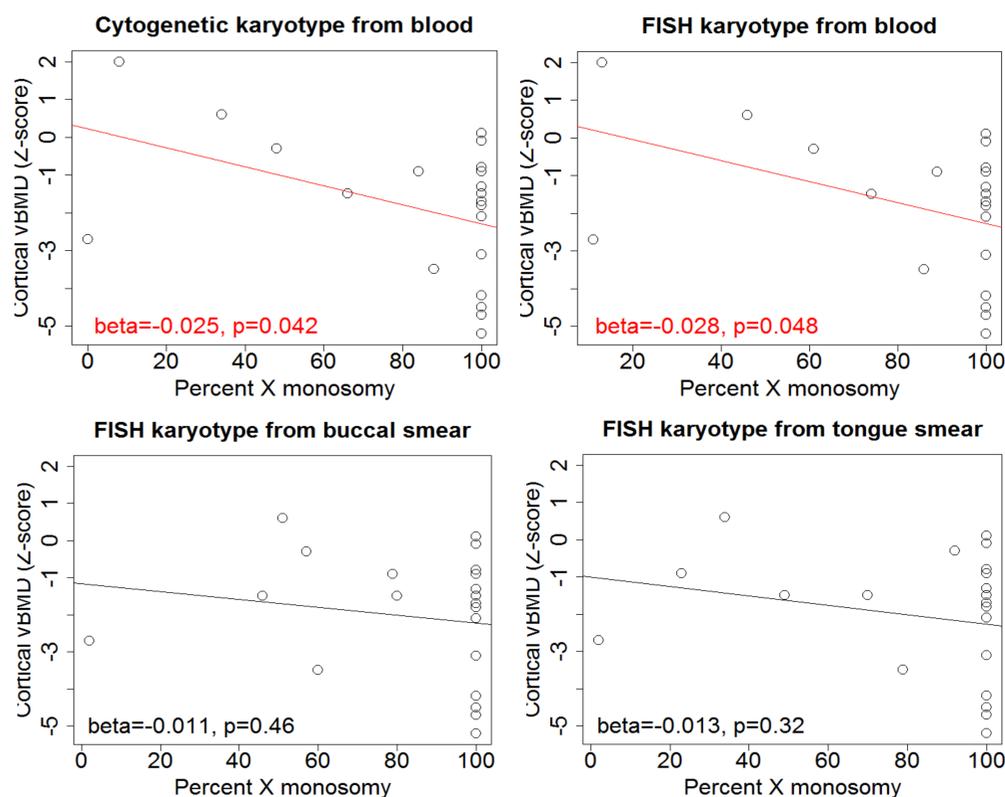
## Methods

Girls with TS who participated in our previous BMD study had new karyotyping. In addition to **classical cytogenetic and molecular (fluorescence in situ hybridization, FISH) karyotyping from lymphocytes (mesoderm origin)**, FISH from cells gained through **buccal (ectoderm origin) and root of tongue (endoderm origin) smears** was also performed. Fifty (cytogenetic) and 250 (FISH) nuclei were analysed, respectively. Percentage of X monosomy was calculated from the proportion of cell line with 45,X.

## Results

“Complete” *SHOX* gene haploinsufficiency was present in 18 girls (45,X monosomy in 15 girls and Xp deletion in both cell lines in 3 girls with mosaicism), whereas in 7 girls the Xp deletion was “partial” due to mosaicism (second cell line presented 46,XX or 46,XY). The remaining 4 girls could not be determined due to ring- or Y-marker chromosome. **One subject presented 45,X monosomy in lymphocytes but had 45,X/47,XXX mosaicism in buccal and root of tongue cells.** The maximum difference in percent X monosomy among the three germ layers was  $37 \pm 18$  (min 15, max 66). Whereas the degree of monosomy did not associate with trabecular BMD (Figure 1), **cortical BMD decreased with higher proportion of 45,X cell line in lymphocytes (Figure 2).**

**Figure 2.**



## Conclusions

The **karyotype result in TS differs by the embryonic origin of the tissue sample.** Despite that the entire skeleton develops from mesoderm, **only the cortical bone compartment had quantitative association with X monosomy in lymphocytes.** Gradual decrease in trabecular vBMD during puberty must have **non-genetic causes.** Knowledge of the karyotype of all three germ layers may help elucidate other tissue specific features of TS.

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