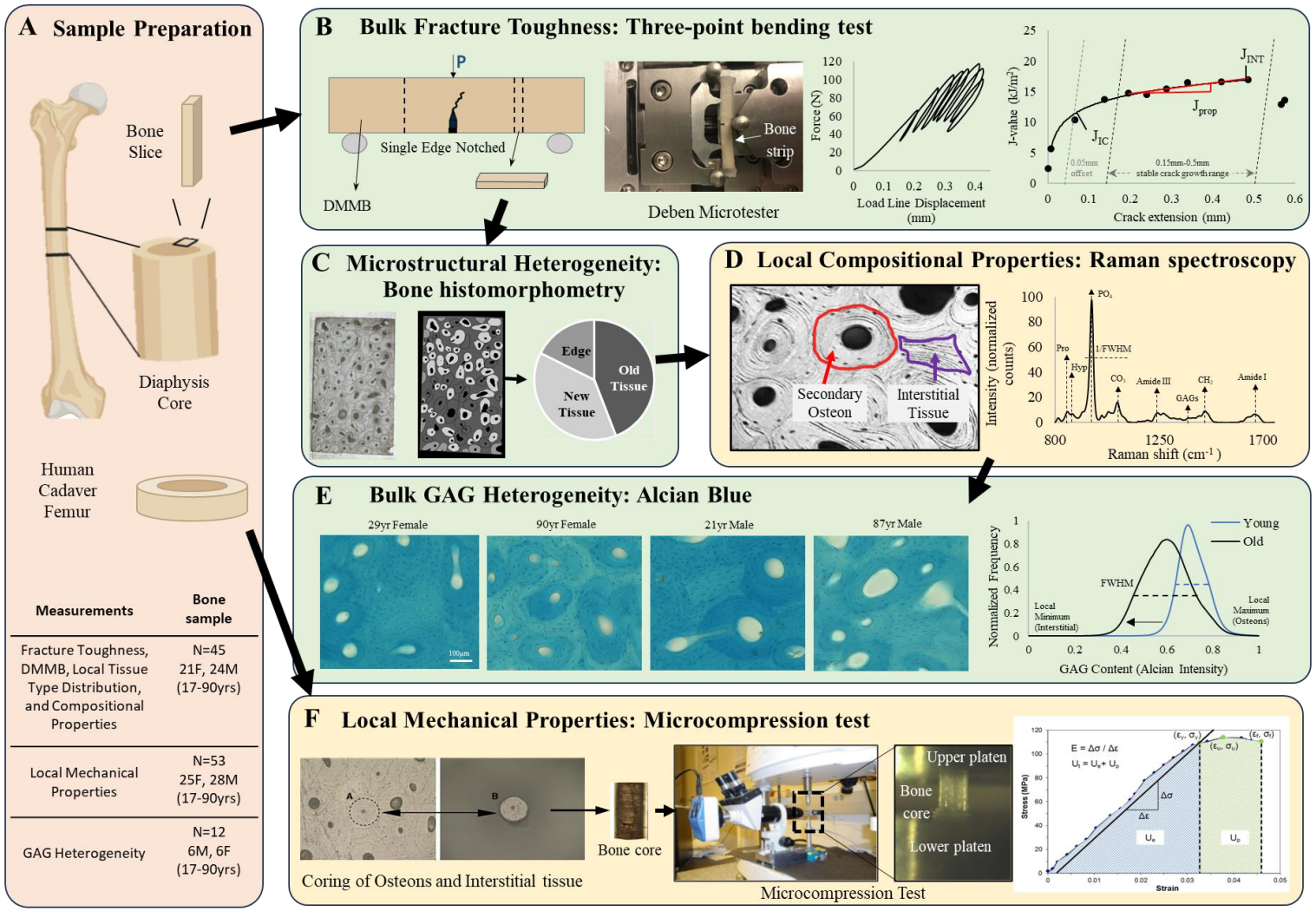
Figure S1. Schematics of experimental setup: **(A)** The diaphysis of human femurs were sectioned into 20x2x4mm^3 rectangular strips aligned in its longitudinal axis for experiments described in B-D, and a 5mm thick cross section slices were dissected for the experiment described in E. **(B)** Three-point fracture toughness tests were conducted on single edge notched specimens in a Deben micromechanical tester to determine R-curves by measuring J-integral using single sample method and estimating crack length using unloading compliance method recommended in ASTM E-1820-A1. **(C)** Bone histomorphometry was used to classify tissue type in the slices from post-fractured specimens. **(D)** Raman spectroscopy was performed to characterize the compositional properties of secondary osteons and interstitial tissue using bone slices obtained from specimens after fracture toughness testing. **(E)** Alcian stained bone sections of young and old male female donors. Histograms of the averaged 6 histograms for young and old donors. **(F)** Microcompression tests were performed to determine mechanical properties of bone cores of secondary osteons and interstitial tissues extracted from the cross-sectional slices.



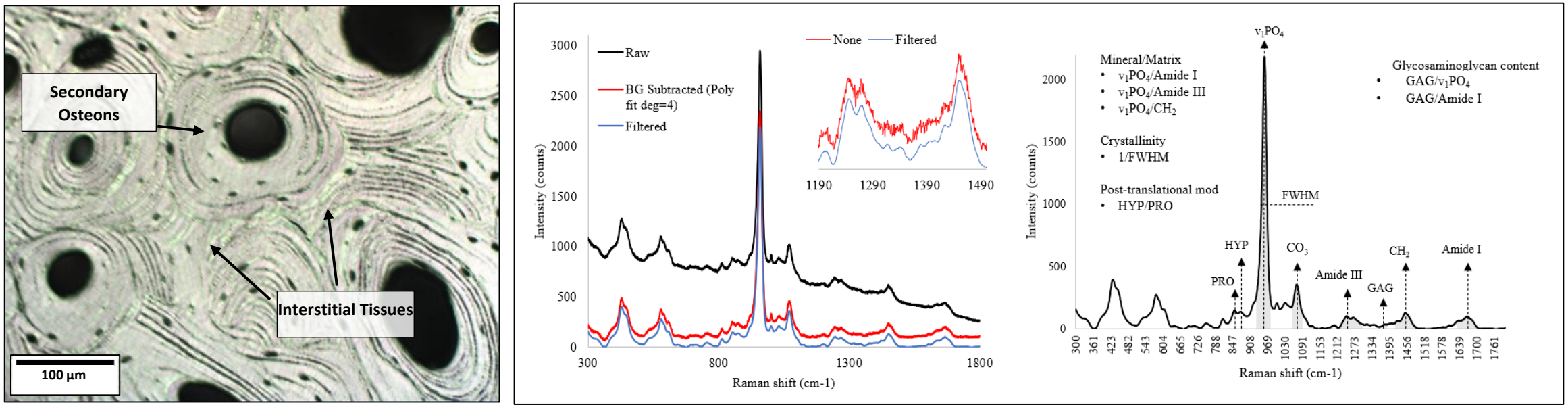


Figure S2. Raman spectroscopy **(A)** Secondary osteons and interstitial tissues for human cortical bone. **(B)** Processing method using peak intensity and integrated area. Raw spectra for each group were averaged (black) and fitted with a 4th order polynomial curve to subtract background fluorescence (BG). Then a S-G filter (2nd order & window size 25) was (blue) and was not (red) applied. **(C)** Peak ratios were used 1) dividing highest peak intensity (PI) by another PI.

Table S1. Table of Donors used per experiment.

Donor ID	Sex	Age Grp	Age	JIC	Jprop	Local Raman	Histomophometry	DMMB	Local Compression Testing	Alcian Blue
1	M	Young	21	Yes	Yes	Yes	Yes	Yes		Yes
2	M	Young	22	Yes	Yes	Yes	Yes	Yes		Yes
3	M	Young	29	Yes		Yes	Yes	Yes		Yes
4	M	Young	30	Yes	Yes	Yes	Yes	Yes		
5	M	Young	36	Yes	Yes	Yes	Yes	Yes	Yes	
6	M	Young	37	Yes	Yes	Yes	Yes	Yes		
7	M	Young	38	Yes	Yes	Yes	Yes	Yes	Yes	
8	M	Mid	47	Yes	Yes	Yes	Yes	Yes	Yes	
9	M	Mid	49	Yes	Yes	Yes	Yes	Yes	Yes	
10	M	Mid	55	Yes	Yes	Yes	Yes	Yes		
11	M	Mid	57	Yes		Yes	Yes	Yes	Yes	
12	M	Mid	59	Yes	Yes	Yes	Yes	Yes	Yes	
13	M	Mid	59	Yes	Yes	Yes	Yes	Yes		
14	M	Elderly	69	Yes		Yes	Yes	Yes	Yes	Yes
15	M	Elderly	71	Yes	Yes	Yes	Yes	Yes		Yes
16	M	Elderly	74	Yes	Yes	Yes	Yes	Yes		
17	M	Elderly	77	Yes	Yes	Yes	Yes	Yes	Yes	
18	M	Elderly	78	Yes		Yes	Yes	Yes		
19	M	Elderly	79	Yes	Yes	Yes	Yes	Yes	Yes	
20	M	Elderly	79	Yes	Yes	Yes	Yes	Yes		
21	M	Elderly	81	Yes	Yes	Yes	Yes	Yes		
22	M	Elderly	83	Yes	Yes	Yes	Yes	Yes		
23	M	Elderly	87	Yes	Yes	Yes	Yes	Yes	Yes	Yes
24	M	Young	20						Yes	
25	M	Young	24						Yes	
26	M	Young	25						Yes	
27	M	Young	26						Yes	
28	M	Young	34						Yes	
29	M	Young	36						Yes	
30	M	Mid	49						Yes	
31	M	Mid	51						Yes	
32	M	Mid	52						Yes	
33	M	Mid	52						Yes	
34	M	Mid	55						Yes	
35	M	Elderly	76						Yes	
36	M	Elderly	76						Yes	
37	M	Elderly	77						Yes	
38	M	Elderly	78						Yes	
39	F	Young	17	Yes	Yes	Yes	Yes	Yes	Yes	Yes
40	F	Young	22	Yes	Yes	Yes	Yes	Yes	Yes	
41	F	Young	25	Yes	Yes	Yes	Yes	Yes	Yes	Yes
42	F	Young	29	Yes	Yes	Yes	Yes	Yes		Yes
43	F	Young	34	Yes	Yes	Yes	Yes	Yes	Yes	
44	F	Mid	46	Yes	Yes	Yes	Yes	Yes	Yes	
45	F	Mid	49	Yes	Yes	Yes	Yes	Yes		
46	F	Mid	51	Yes	Yes	Yes	Yes	Yes	Yes	
47	F	Mid	51	Yes		Yes	Yes	Yes	Yes	
48	F	Mid	52	Yes	Yes	Yes	Yes	Yes		
49	F	Mid	53	Yes	Yes	Yes	Yes	Yes	Yes	
50	F	Mid	54	Yes	Yes	Yes	Yes	Yes	Yes	
51	F	Mid	54	Yes		Yes	Yes	Yes	Yes	
52	F	Mid	54	Yes	Yes	Yes	Yes	Yes		
53	F	Elderly	73	Yes	Yes	Yes	Yes	Yes		
54	F	Elderly	78	Yes	Yes	Yes	Yes	Yes		Yes
55	F	Elderly	81	Yes	Yes	Yes	Yes	Yes	Yes	Yes
56	F	Elderly	81	Yes	Yes	Yes	Yes	Yes	Yes	
57	F	Elderly	86	Yes	Yes	Yes	Yes	Yes		
58	F	Elderly	88	Yes	Yes	Yes	Yes	Yes	Yes	
59	F	Elderly	90	Yes	Yes	Yes	Yes	Yes	Yes	Yes
60	F	Young	26						Yes	
61	F	Mid	42						Yes	
62	F	Mid	43						Yes	
63	F	Mid	47						Yes	
64	F	Mid	56						Yes	
65	F	Mid	63						Yes	
66	F	Elderly	68						Yes	
67	F	Elderly	73						Yes	
68	F	Elderly	74						Yes	
69	F	Elderly	84						Yes	
70	F	Elderly	88						Yes	
71	F	Elderly	89						Yes	

Table S2. Compositional and mechanical properties of secondary osteons and interstitial tissue (mean ± standard deviation)

Sex	Donor Age	Tissue Type	Mineral Matrix Ratios				Mineral Quality		Organic Quality				
			PO_4/CH_2	PO_4/Amide I	PO_4/Amide III	PO_4/Pro	CO_3 content	Crystallinity (1/FWHM PO_4)	**GAG/PO_4**	**GAG/ Amide I**	Helical Status (1665/1635)	Matrix Maturity (1665/1690)	Hyp/Pro
Female	Young (17-34yrs)	Osteon	10.5 ± 0.73	13.32 ± 1.28	12.27 ± 0.78	12.92 ± 0.96	0.175 ± 0.011	0.0641 ± 0.0006	**0.034 ± 0.007**	**0.13 ± 0. 032**	1.52 ± 0.04	1.91 ± 0.08	1.24 ± 0.03
		Interstitial	11.9 ± 0.61	16.02 ± 1.9	13.27 ± 0.55	14.2 ± 0.72	0.168 ± 0.005	0.0644 ± 0.0004	**0.033 ± 0.003**	**0.106 ± 0. 029**	1.6 ± 0.04	1.9 ± 0.08	1.24 ± 0.03
	Middle (46-60yrs)	Osteon	9.93 ± 0.58	11.91 ± 0.83	11.88 ± 0.83	12.48 ± 0.85	0.193 ± 0.01	0.0635 ± 0.0009	**0.038 ± 0.005**	**0.122 ± 0. 024**	1.55 ± 0.03	1.84 ± 0.12	1.24 ± 0.03
		Interstitial	12.02 ± 0.61	15.1 ± 1.52	14.4 ± 0.73	14.84 ± 0.79	0.178 ± 0.004	0.0643 ± 0.0005	**0.03 ± 0.003**	**0.114 ± 0. 017**	1.56 ± 0.02	1.82 ± 0.13	1.24 ± 0.03
	Elderly (73-90yrs)	Osteon	10.2 ± 0.26	12.13 ± 0.71	11.84 ± 0.49	12.42 ± 0.44	0.196 ± 0.009	0.0635 ± 0.0007	**0.033 ± 0.004**	**0.132 ± 0. 02**	1.53 ± 0.05	1.81 ± 0.06	1.22 ± 0.05
		Interstitial	11.78 ± 0.6	14.46 ± 1.07	13.51 ± 0.68	13.9 ± 0.97	0.181 ± 0.005	0.0644 ± 0.0002	**0.028 ± 0.001**	**0.131 ± 0. 029**	1.56 ± 0.04	1.83 ± 0.06	1.22 ± 0.05
Male	Young (20-38yrs)	Osteon	10.61 ± 0.72	13.39 ± 1.45	12.3 ± 0.68	13.07 ± 1.05	0.178 ± 0.012	0.0642 ± 0.0015	**0.035 ± 0.006**	**0.126 ± 0. 024**	1.57 ± 0.04	1.82 ± 0.16	1.22 ± 0.01
		Interstitial	12.24 ± 0.67	16.09 ± 1.96	14.29 ± 0.64	14.49 ± 1.4	0.173 ± 0.008	0.0641 ± 0.0008	**0.031 ± 0.002**	**0.118 ± 0. 034**	1.61 ± 0.04	1.82 ± 0.14	1.22 ± 0.01
	Middle (43-59yrs)	Osteon	10.21 ± 0.59	12.69 ± 1.14	12.24 ± 0.58	12.61 ± 0.77	0.192 ± 0.009	0.063 ± 0.0007	**0.038 ± 0.006**	**0.142 ± 0. 016**	1.57 ± 0.05	1.72 ± 0.08	1.25 ± 0.05
		Interstitial	11.74 ± 1.14	15.18 ± 2.33	14.15 ± 1.62	14.8 ± 1.96	0.176 ± 0.005	0.0641 ± 0.0008	**0.034 ± 0.005**	**0.11 ± 0. 015**	1.59 ± 0.06	1.75 ± 0.1	1.25 ± 0.05
	Elderly (69-87yrs)	Osteon	10.02 ± 0.37	12.39 ± 1.01	11.77 ± 0.4	12.33 ± 0.61	0.194 ± 0.003	0.0636 ± 0.0003	**0.038 ± 0.005**	**0.143 ± 0. 028**	1.59 ± 0.04	1.9 ± 0.15	1.23 ± 0.05
		Interstitial	11.99 ± 0.82	15.41 ± 0.67	14.17 ± 0.75	14.89 ± 0.84	0.181 ± 0.002	0.0644 ± 0.0003	**0.035 ± 0.007**	**0.127 ± 0. 038**	1.59 ± 0.04	1.88 ± 0.15	1.23 ± 0.05

Sex	Donor Age	Tissue Type	Mechanical Properties of Local Tissues									
			Yield Stress (MPa)	Yield Strain (mm/mm)	Elastic Modulus (GPa)	Failure Stress (MPa)	Failure Strain (mm/mm)	Elastic Energy (MJ)	Plastic Energy (MJ)	Toughness (MJ)	Ult. Stress (MPa)	Ult. Strain (mm/mm)
Female	Young (17-34yrs)	Osteon	94.1±40.4	0.04±0.01	3.01±1.77	97.3±35.1	0.28±0.12	1.89±0.64	29.8±6.47	31.6±7.06	118±42.3	0.11±0.05
		Interstitial	111±27.8	0.03±0	4.02±1.76	102±21.5	0.26±0.04	2.04±0.1	29.4±13.4	31.4±13.45	145±46.1	0.11±0.03
	Middle (42-63yrs)	Osteon	96.8±46.2	0.03±0.01	3.23±1.85	65.2±18.4	0.33±0.08	1.98±0.83	33.5±14.48	35.4±15.1	123±35.8	0.14±0.08
		Interstitial	101±14.0	0.04±0.01	3.09±0.87	85.7±10.75	0.24±0.03	2.43±1.28	20.9±4.51	23.4±4.92	117±20.8	0.09±0.02
	Elderly (68-90yrs)	Osteon	103±35.1	0.04±0.01	3.55±1.82	115±44.8	0.31±0.06	2.16±0.84	29.1±12.2	31.3±12.7	116.33.1	0.08±0.05
		Interstitial	100±33.0	0.04±0	2.96±1.01	107±39.7	0.25±0.04	2.31±0.89	20.7±5.80	23.0±6.22	121±31.4	0.1±0.05
Male	Young (20-38yrs)	Osteon	87.5±375	0.04±0.01	2.69±1.62	83.0±30.3	0.32±0.07	1.9±0.93	28.1±13.15	30.0±13.6	108±46.4	0.14±0.05
		Interstitial	108±27.5	0.03±0	3.68±1.2	85.8±15.2	0.23±0.05	2.09±0.55	23.0±7.90	25.1±8.03	133±23.5	0.11±0.05
	Middle (47-59yrs)	Osteon	93.0±36.28	0.05±0.02	3.04±1.4	83.6±31.7	0.32±0.04	2.2±1.21	28.1±6.92	30.3±7.24	116±33.9	0.15±0.1
		Interstitial	101±16.0	0.04±0.01	3.04±0.93	93.8±30.4	0.25±0.04	2.49±0.74	22.0±5.30	24.5±5.91	126±16.8	0.11±0.04
	Elderly (69-87yrs)	Osteon	73.7±36.4	0.04±0.02	2.5±1.41	74.1±21.1	0.33±0.07	1.71±0.94	25.3±6.87	27.0±7.31	94.7±32.2	0.12±0.06
		Interstitial	82.4±24.3	0.04±0.01	2.55±0.88	75.5±25.3	0.25±0.05	1.99±0.57	19.5±5.67	21.5±5.76	108±29.4	0.11±0.03

Table S3. Effects of age and sex on the distribution of tissue types and GAGs in bone cross-section (mean ± standard deviation)

Test Groups		**% New Tissue**	**Tissue Age Ratio ($R_{N/O}$)**	**% Porosity**	**Bulk GAG DMMB** (ng/mg)	**Bulk GAG Alcian** (normalized intensity)	**FWHM**
Female	Young	0.16 ± 0.05	0.22 ± 0.09	0.05 ± 0.01	1470 ± 201	0.83 ± 0.07	13.33 ± 3.06
	Mid	0.18 ± 0.02	0.25 ± 0.04	0.07 ± 0.03	1339 ± 112	--	--
	Elderly	0.11 ± 0.03	0.15 ± 0.05	0.09 ± 0.04	1162 ± 224	0.68 ± 0.07	24.00 ± 3.61
Male	Young	0.18 ± 0.03	0.24 ± 0.05	0.05 ± 0.02	1369 ± 235	0.84 ± 0.03	13.33 ± 2.89
	Mid	0.13 ± 0.04	0.19 ± 0.06	0.07 ± 0.03	1469 ± 253	--	--
	Elderly	0.14 ± 0.04	0.19 ± 0.07	0.1 ± 0.04	1298 ± 135	0.76 ± 0.03	20.00 ± 1.73

Table S4. Descriptive statistics (mean ± standard deviation) of the bulk fracture toughness of bone.

Test Groups		**J_{IC}** (kJ/m^2)	**J_{PROP}** (kJ/m^3)
Female	Young	13.62 ± 3.40	66.78 ± 13.97
	Mid-aged	11.70 ± 2.51	35.44 ± 11.87
	Elderly	10.80 ± 2.52	33.69 ± 15.67
Male	Young	13.74 ± 2.41	35.48 ± 20.50
	Mid-aged	13.00 ± 2.42	28.44 ± 12.94
	Elderly	11.86 ± 3.12	28.96 ± 12.84