Published in final edited form as:

Nutr Cancer. 2018 January ; 70(1): 45–50. doi:10.1080/01635581.2018.1412479.

Are Circulating Phospholipid Fatty Acids a Reasonable Surrogate for Target Tissue Levels In The Prostate?

Jeannette M. Schenk^a, Xiaoling Song^a, Colm Morrissey^b, Robert L. Vessella^b, Daniel W. Lin^{a,b}, and Marian L. Neuhouser^a

^aFred Hutchinson Cancer Research Center, Cancer Prevention Program,

^bUniversity of Washington, Department of Urology

Abstract

Inconsistent results from epidemiologic studies of circulating fatty acids and prostate cancer risk may be partly due to use of blood concentrations as surrogate biomarkers of prostate tissue concentrations. To determine whether blood concentrations reflect prostate tissue fatty acid profiles, we evaluated associations between phospholipid fatty acid (PLFA) profiles measured in plasma and prostate tissue from 20 patients who underwent prostatectomy. For each patient, three prostate tissue specimens varying in size and location were collected. Correlations were calculated between a) tissue specimens by size (< 20 mg, >20 mg); b) individual tissue samples (Intraclass Correlation Coefficient (ICC)); and c) plasma and mean tissue PLFA concentrations. PLFA concentrations from < 20 mg and >20 mg tissues were nearly identical. For most PLFAs, intra-individual correlations between tissue specimens were moderate to strong (linoleic acid=0.66, eicosapentaenoic acid=0.96), with only one ICC below 0.50 (trans-fatty acid 18:2, ICC=0.28). Most correlations of mean tissue and plasma concentrations were moderate to strong (α -linoleic acid=0.47, eicosapentaenoic acid=0.93). PLFA concentrations are largely homogeneous within the prostate and can be reliably measured in small quantities of tissue. The overall strong correlations between plasma and tissue suggest that for most individual PLFAs, plasma concentrations are adequate surrogate markers of prostate tissue concentrations.

Keywords

prostate; phospholipid fatty acids; omega-3 fatty acids; biomarker

INTRODUCTION

The relationship between polyunsaturated fatty acids (PUFA) and prostate cancer risk remains elusive. ω -3 PUFA have well-established anti-inflammatory properties (1), and high levels of these fatty acids show protective effects against prostate cancer in a number of

Corresponding Author: Jeannette M. Schenk, 1100 Fairview Ave N., M4-B402, Seattle, WA 98199-1024, Office: 206.667.6860, Cell: 206.284.3225, jschenk@fredhutch.org.

Statement of authors' contributions to manuscript: J.M.S. and M.L.N. designed research; J.M.S., X.S., M.L.N., C.M., R.L.V., and D.W.L. conducted research, J.M.S. analyzed data, J.M.S., M.L.N., and X.S. wrote paper; J.M.S. had primary responsibility for final content. All authors have read and approved the final manuscript.

Conflict of Interest: The authors declare no potential conflicts of interest.

experimental systems, including in-vitro, synthetic cell lines and transplantable human prostate tumors.(2-4) However, results from epidemiologic studies have been inconsistent. Human observational studies of self-reported dietary intake(5) suggest that consumption of fish or marine ω -3 PUFA may reduce prostate cancer incidence, recurrence, or mortality. However, among cohort studies based on circulating fatty acid concentrations, the majority reported no associations for the long-chain ω -3 fatty acids EPA (20:5 ω -3) and DHA(22:6 ω -3), and several reported increased risk for α -linolenic acid (18:3 ω -3) and total prostate cancer risk.(6-8) More recently, two highly-publicized studies from large cohorts of men [Prostate Cancer Prevention Trial (PCPT) and Selenium and Vitamin E Cancer Trial (SELECT)] reported that higher vs lower circulating phospholipid ω -3 PUFAs were associated with a 1.71 to 2.50 fold increase in the risk of high-grade prostate cancer (Gleason 7).(9, 10)

Inconsistent associations of ω -3 and prostate cancer may in part be due to use of circulating ω -3 PUFAs as surrogate biomarkers for the fatty acid profile of target (prostate) tissues. The relationship between blood and prostate tissue PUFAs is unknown. Few studies have measured prostate tissue fatty acid profiles, and little is known about the reliability of these measurements.(11-13) Given that the target (prostate) tissue is the major point of clinical interest, it is important to determine whether use of blood biomarkers is the correct scientific approach for testing associations of PUFAs with prostate cancer risk and/or progression.

MATERIALS AND METHODS

Twenty patients were randomly selected from the University of Washington Genitourinary Cancer Repository who met the following criteria: had biopsy-determined prostate cancer; underwent prostatectomy; and consented to the collection and storage of fasting blood and tissue specimens not needed for diagnostic purposes. Data on clinical and participant characteristics, and plasma and prostate tissue samples were obtained from the repository for each participant. For each participant, three separate OCT embedded tissue blocks from the peripheral zone of the prostate and not containing cancer were selected. Because PUFA concentrations may be altered in prostate cancer, normal prostate tissue was used for this study. Tissue blocks were first processed to remove all OCT, then one sample was collected in each block. Tissue samples varied in size (10 mg to 50 mg), which was estimated based on the size and thickness of the tissue piece. All patients signed written informed consent under an approved IRB protocol at the University of Washington Medical Center at the time of blood and tissue donation.

PUFA measurement methods:

De-identified prostate tissue and plasma phospholipid fatty acid (PLFA) profiles were analyzed in the Fred Hutchinson Cancer Research Center's Public Health Sciences Biomarker Laboratory, which maintains on-going IRB approval for the assay of human biological specimens without identifiers. The plasma PLFA assay has been described previously.(14) Briefly, total lipids were extracted from plasma using the method of Folch.(15) Phospholipids were separated from other lipids by one dimensional thin layer chromatography.(16) Fatty acid methyl esters of the phospholipids were prepared by direct

transesterification(17) and separated using gas chromatography (Agilent 5890 Gas Chromatograph with flame ionization detector, Supelco fused silica 100m capillary column SP-2560). This GC method quantified 41 known fatty acids for this study. For prostate tissue, each sample was first homogenized in solution A (2:1 Chloroform: Methanol) using 5mm stainless steel bead and TissueLyzer with an LT adapter, then the protocol used for plasma samples was followed. Relative concentration of each fatty acid was expressed as a weight percentage of the total sum of PLFAs analyzed. PLFA profiles were measured in a single 0.2ml aliquot of plasma, and in each tissue sample separately. Inter-assay coefficients of variation for these PLFAs, as measured in pooled plasma QC samples, were all less than 5%. Tissue samples were not available for QC of prostate PLFA profiles.

Here we report a selected subset of phospholipid PUFAs, including Eicosapentaenoic acid (EPA; 20:5 ω 3), Docosahexaenoic acid (DHA; 22:6 ω 3), Docosapentaenoic acid (DPA; 22:5 ω 3), Alpha-linoleic acid (ALA; 18: 3 ω 3), Linoleic acid (LA; 18:2 ω 6), Arachidonic acid (AA; 20:4 ω 6), and trans-fatty acids (TFA), for which associations with prostate cancer have been previously reported.(6-10)

Statistical Analyses

The overall goal of these analyses was to determine whether prostate tissue PLFAs could be measured, and whether circulating profiles reflect tissue PLFA profiles. Total long-chain ω -3 PLFA for tissue and plasma was calculated as the sum of EPA, DPA and DHA, and because of their low concentrations, trans-fatty acids were grouped as trans-16:1 (16:1 ω 7t + 16:1 ω 9t), trans-18:1 (18:1 ω 6t + 18:1 ω 7t + 18:1 ω 8t + 18:1 ω 9t + 18:1 ω 10-12t) and trans-18:2 (18:2 ω 6tt + 18:2 ω 6ct + 18:2c6tc). For prostate tissue PLFA profiles, means and standard deviations of each PLFA were calculated by weight of tissue specimen ($\leq$ 20 mg vs $>$ 20 mg). To evaluate correlations of tissue PLFAs between specimens $\leq$ 20 mg and $>$ 20 mg, Pearson, Partial Pearson (adjusted for age) correlation coefficients were reported. In addition, Intraclass Correlation Coefficients (ICC) and coefficients of variation (CV) were used to evaluate the reliability of prostate tissue PLFA from three distinct specimens of each participant. For plasma, mean relative concentrations and standard deviations were calculated for each PLFA. For prostate tissue, means of PLFA concentrations from the three distinct tissue specimens were also calculated for each participant. To evaluate correlations of PLFAs between plasma and prostate tissue (overall), Pearson and Partial Pearson (adjusted for age) correlation coefficients were reported. Statistical analyses were performed using SAS version 9.3 software (SAS Institute, Cary, NC). All statistical tests are two-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

Tissue specimens were from men who were primarily Caucasian (85%), never smokers (60%), had no family history of prostate cancer (75%), and were an average of 59.7 ($\pm$ 7.4) years old (data not shown).

Table 1 gives mean prostate tissue PLFA profiles from specimens $\leq$ 20 mg and $>$ 20 mg. Mean PUFA concentrations in tissue specimens $\leq$ 20 mg were nearly identical to those in specimens $>$ 20 mg. Correlations of PUFA concentrations from specimens $\leq$ 20 mg and $>$ 20

mg ranged from 0.10 to 0.99 (Table 1). Correlations between tissue specimens of varying size were strongest for ω -3 fatty acids, ranging from 0.67 for ALA to 0.95 for total omega-3 and 0.99 for EPA. For selected trans-fatty acid concentrations, correlations between specimens ≤ 20 mg and >20 mg varied substantially, ranging from 0.10 for trans-18:2, to 0.83 for trans-18:1. Correlations for individual omega-6 fatty acid concentrations were moderate (0.51 to 0.72), although still statistically significant. The magnitude of Pearson and age-adjusted Pearson correlations was comparable.

Intraclass Correlation Coefficients (ICCs) comparing tissue PLFA concentrations from three distinct specimens per participant are given in Table 2. For most individual fatty acids, the ICC was moderate to strong, ranging from 0.66 for linoleic acid to 0.96 for eicosapentaenoic acid, with only one ICC below 0.50 (TFA 18:2: ICC=0.28). Mean coefficients of variation (CV) between the three distinct tissue specimens were all < 0.16 (Table 2).

Table 3 gives mean concentrations of PUFAs in plasma and prostate tissue using the mean of 3 non-malignant tissue specimens from each participant. Overall, most but not all fatty acid concentrations were lower in tissue than in plasma. Both Pearson and Partial Pearson correlations between plasma and tissue PUFA concentrations were moderate or strong for almost all selected PUFAs. Correlations between plasma and tissue concentrations were strongest for EPA (0.93) and total ω -3 fatty acids (Pearson $r=0.90$); however, for ALA, the correlation between plasma and tissue was very poor (Pearson $r=0.03$).

DISCUSSION

In this study we demonstrated the feasibility and reliability of measuring phospholipid fatty acid profiles in prostate tissue samples, and showed that for most PLFA, prostate tissue concentrations are highly correlated with circulating plasma concentrations. The overall moderate to strong correlations between plasma and tissue concentrations for most individual PLFAs, though not all, suggest that plasma PLFA profiles are adequate surrogate markers of target (prostate) tissue PLFA profiles.

To our knowledge, only three studies have previously reported PUFA concentrations in prostate tissue specimens.(11-13) Two of these studies were based on prostatectomy specimens, from which a large amount of prostate tissue is available(11, 12), and one recent study by Moreel et al. measured prostate tissue fatty acid concentrations from a single prostate biopsy core in 29 men(13). Although the prostate tissue specimens tested for the present study were slightly larger than the typical 5 mg biopsy core, the mean tissue fatty acid concentrations in our sample were similar to those reported by Moreel et al. In the present study we also found that PUFA concentrations in smaller tissue samples (≤ 20 mg) were nearly identical to concentrations in larger tissue samples (>20 mg) from the same participant, and that mean concentrations of individual fatty acid concentrations were not significantly different between smaller and larger tissue samples (all P -values >0.05). Together, these data demonstrate that fatty acid profiles can be feasibly measured in prostate tissue and that the assay is sensitive enough to measure PLFA profiles in small quantities of prostate tissue.

To evaluate the possible effect of tissue heterogeneity on measurement of PLFA profiles in prostate tissue, for each participant we measured PUFA concentrations in three separate prostate tissue specimens taken from distinct prostate tissue blocks. We found that the concentrations for most individual PLFAs, with the exception of 18:2 TFA, were highly correlated between the three samples with ICC's ranging from 0.66 for Linoleic acid to 0.96 for eicosapentaenoic acid. Furthermore, the correlations of fatty acid concentrations between the individual tissue samples did not appear differ substantially by the class or concentration of fatty acid measured. These results suggest that fatty acid profiles are largely homogeneous within the prostate gland.

To evaluate whether circulating fatty acid profiles are a suitable biomarker of tissue phospholipid fatty acid concentrations, we reported the associations of plasma and tissue concentrations of several selected phospholipid fatty acids. For the majority of PLFAs selected, circulating PLFA concentrations are good surrogate markers for prostate tissue PLFA concentrations; however, the strength of the correlations between PLFA concentrations from plasma and tissue did vary by fatty acid. For most omega-3 fatty acids, correlations between circulating and tissue concentrations were excellent; however, for ALA, the correlation between plasma and tissue was poor ($r=0.03$). It is possible that the low correlation may be partially explained by the low concentration of this fatty acid in the both plasma and tissue; although other fatty acids were detected in similarly low concentrations and had much higher correlations between blood and tissue (ie 16:1 and 18:2TFA). The correlation of plasma and prostate tissue EPA concentrations (0.93) was much higher than recently reported by Moreel (0.58). It is possible that differences in the correlations may be due to the measurement of prostate tissue fatty acids in phospholipids (the present study) versus total lipids, or due to the measurement of circulating plasma PLFA (the present study) versus RBC PLFA.(13) The

These results suggest that most circulating fatty acid concentrations are good surrogate markers of benign prostate tissue fatty acid profiles, and that the inconsistencies in associations of PLFA and prostate cancer risk in the epidemiologic literature may not be related to the use of blood concentrations as surrogate markers. Given the strong correlation between circulating and tissue PLFA concentrations for most fatty acids, the use of circulating levels as a surrogate would have only a small impact on the true risk estimate. However, for some specific fatty acids, such as ALA or TFA 18:2, which have low correlation between circulating and tissue levels, the use of circulating concentrations could substantially attenuate the risk estimate towards the null (assuming non-differential measurement error).

Some limitations of this study are worth mentioning. First, the sample size was small; nevertheless, the weight of prostate tissue samples was approximated based on the size and thickness of the specimens that were cut from the block; thus, analyses based on tissue size were somewhat crude (< 20 mg and > 20 mg). Second, homogenous replicate tissue samples were not available to directly assess the reproducibility of the prostate PLFA assay. Moreel et al. previously reported relatively high coefficients of variation (CV) between two distinct biopsy cores for several prostate tissue fatty acids (range 0.15 (linoleic) to 0.60 (alpha-linoleic acid))(13). However, for the three distinct tissue specimens used in this study,

calculated mean CVs were all < 0.16 [range: 0.04 (docosahexanoic acid) to 0.16 (alpha-linoleic acid)], suggesting the PLFA assay is reproducible for tissue samples. Third, because only plasma was available, we were unable to measure red blood cell fatty acids, which are commonly measured to characterize longer-term dietary exposure. However, phospholipids exchange between plasma and red blood cell membranes(18), plasma PLFA concentrations are moderate to highly correlated with red blood cell fatty acid concentrations(18-20), and have parallel responses to dietary intervention(21); thus plasma PLFAs are also considered a comparable biomarker. Lastly, due to the relatively small sample size and lack of covariate data, we were not able to determine whether there were any differences in correlations between patient subgroups.

CONCLUSION

In conclusion, the results of this exploratory study suggest that phospholipid fatty acid profiles can be feasibly and reliably measured in prostate tissue, and that the size and location of the tissue sample may not affect overall measurement of prostate tissue phospholipid fatty acid concentrations. Furthermore, given the overall strong correlations between plasma and tissue concentrations for most individual PLFAs, most, though not all, plasma PLFA concentrations are adequate surrogate markers of target (prostate) tissue PLFA concentrations. Future directions in this area of research could include evaluating whether ω -3 PUFA concentrations differ between benign and cancerous prostate tissue in larger sample sets in order to further unravel the inconsistent and unexplained associations of plasma PLFA and prostate cancer risk.

Acknowledgements:

We would like to acknowledge the participating patients, and physicians: Drs. Paul Lange, Jonathan Wright, William Ellis, Bruce Dalkin, and John Gore. We would also like to thank Dr. Lawrence True, Jennifer Noteboom, Lori Kollath, and the tissue acquisition team in the Department of Urology, School of Medicine, University of Washington

Financial Support: This study is the result of work supported by the Pacific Northwest Prostate Cancer SPORE (P50CA97186) and by the Fred Hutchinson Cancer Research Center.

REFERENCES

1. Chapkin RS, Kim W, Lupton JR, McMurray DN. 2009 Dietary docosahexaenoic and eicosapentaenoic acid: emerging mediators of inflammation. *Prostaglandins Leukot Essent Fatty Acids*, 81: 187–191. [PubMed: 19502020]
2. Pandalai P, Pilat M, Yamazaki K, Naik H, Pienta K. 1995 The effects of omega-3 and omega-6 fatty acids on in vitro prostate cancer growth. *Anticancer Res*, 16: 815–820.
3. Rose DP, Connolly JM. 1991 Effects of fatty acids and eicosanoid synthesis inhibitors on the growth of two human prostate cancer cell lines. *Prostate*, 18: 243–254. [PubMed: 2020620]
4. Karmali R, Reichel P, Cohen L, Terano T, Hirai A et al. 1986 The effects of dietary omega-3 fatty acids on the DU-145 transplantable human prostatic tumor. *Anticancer Res*, 7: 1173–1179.
5. Szymanski KM, Wheeler DC, Mucci LA. 2010 Fish consumption and prostate cancer risk: a review and meta-analysis. *Am J Clin Nutr*, 92: 1223–1233. [PubMed: 20844069]
6. Gann PH, Hennekens CH, Sacks FM, Grodstein F, Giovannucci EL et al. 1994 Prospective study of plasma fatty acids and risk of prostate cancer. *J Natl Cancer Inst*, 86: 281–286. [PubMed: 8158682]

7. Laaksonen DE, Laukkanen JA, Niskanen L, Nyyssonen K, Rissanen TH et al. 2004 Serum linoleic and total polyunsaturated fatty acids in relation to prostate and other cancers: a population-based cohort study. *Int J Cancer*, 111: 444–450. [PubMed: 15221975]
8. Harvei S, Bjerve KS, Tretli S, Jellum E, Robsahm TE et al. 1997 Prediagnostic level of fatty acids in serum phospholipids: O-3 and O-6 fatty acids and the risk of prostate cancer. *Int J Cancer*, 71: 545–551. [PubMed: 9178806]
9. Brasky TM, Darke AK, Song X, Tangen CM, Goodman PJ et al. 2013 Plasma phospholipid fatty acids and prostate cancer risk in the SELECT trial. *J Natl Cancer Inst*, 105: 1132–1141. [PubMed: 23843441]
10. Brasky TM, Till C, White E, Neuhaus ML, Song X et al. 2011 Serum phospholipid fatty acids and prostate cancer risk: results from the prostate cancer prevention trial. *Am J Epidemiol*, 173: 1429–1439. [PubMed: 21518693]
11. Aronson WJ, Kobayashi N, Barnard RJ, Henning S, Huang M et al. 2011 Phase II prospective randomized trial of a low-fat diet with fish oil supplementation in men undergoing radical prostatectomy. *Cancer Prev Res (Phila)*, 4: 2062–2071. [PubMed: 22027686]
12. Demark-Wahnefried W, Polascik TJ, George SL, Switzer BR, Madden JF et al. 2008 Flaxseed supplementation (not dietary fat restriction) reduces prostate cancer proliferation rates in men presurgery. *Cancer Epidemiol Biomarkers Prev*, 17: 3577–3587. [PubMed: 19064574]
13. Moreel X, Allaire J, Leger C, Caron A, Labonte ME et al. 2014 Prostatic and dietary omega-3 fatty acids and prostate cancer progression during active surveillance. *Cancer Prev Res (Phila)*, 7: 766–776. [PubMed: 24824038]
14. Reinders I, Song X, Visser M, Eiriksdottir G, Gudnason V et al. 2015 Plasma phospholipid PUFAs are associated with greater muscle and knee extension strength but not with changes in muscle parameters in older adults. *J Nutr*, 145: 105–112. [PubMed: 25355842]
15. Folch J, Lees M, Sloane-Stanley G. 1957 A simple method for the isolation and purification of total lipids from animal tissues. *J Biol Chem*, 226: 497–509. [PubMed: 13428781]
16. Schlierf G, Wood P. 1965 Quantitative Determination of Plasma Free Fatty Acids and Triglycerides by Thin-Layer Chromatography. *J Lipid Res*, 6: 317–319. [PubMed: 14328439]
17. Lepage G, Roy CC. 1986 Direct transesterification of all classes of lipids in a one-step reaction. *J Lipid Res*, 27: 114–120. [PubMed: 3958609]
18. Haest CWM. Distribution and Movement of Membrane Lipids Red Cell Membrane Transport in Health and Disease. Bernhardt I, Ellory JC (eds). Berlin, Germany: Springer Berlin Heidelberg, 2003, pp 1–25.
19. Patel PS, Sharp SJ, Jansen E, Luben RN, Khaw KT et al. 2010 Fatty acids measured in plasma and erythrocyte-membrane phospholipids and derived by food-frequency questionnaire and the risk of new-onset type 2 diabetes: a pilot study in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk cohort. *Am J Clin Nutr*, 92: 1214–1222. [PubMed: 20861175]
20. Phillips GB, Dodge JT. 1967 Composition of phospholipids and of phospholipid fatty acids of human plasma. *J Lipid Res*, 8: 676–681. [PubMed: 6057496]
21. Hodson L, Skeaff CM, Fielding BA. 2008 Fatty acid composition of adipose tissue and blood in humans and its use as a biomarker of dietary intake. *Prog Lipid Res*, 47: 348–380. [PubMed: 18435934]

Table 1.

Relative concentrations of tissue phospholipid fatty acids by tissue sample size, and correlations of concentrations from non-malignant prostate tissue specimens 20 mg and > 20 mg.

	Tissue size		Correlations		P-value ^b
	20 mg Mean ± SD	>20 mg Mean ± SD	Pearson	Partial Pearson ^a	
ω-3 fatty acids					
α-linoleic acid (18:3ω3)	0.24 ± 0.08	0.23 ± 0.08	0.67 ^c	0.63 ^c	0.82
EPA(20:5ω3)	0.20 ± 0.11	0.19 ± 0.10	0.99 ^d	0.96 ^d	0.04
DPA(22:5ω3)	0.97 ± 0.20	1.0 ± 0.24	0.78 ^e	0.78 ^e	0.84
DHA (22:6ω3)	2.67 ± 0.61	2.67 ± 0.54	0.95 ^d	0.95 ^d	0.78
Total ω-3 (EPA + DPA + DHA)	3.84 ± 0.81	3.86 ± 0.76	0.95 ^d	0.94 ^d	0.86
ω-6 fatty acids					
Linoleic Acid (18:2ω6)	7.27 ± 0.89	7.57 ± 1.24	0.51 ^c	0.53 ^c	0.81
Arachidonic Acid (20:4ω6)	13.99 ± 1.59	14.03 ± 1.62	0.72 ^e	0.72 ^e	0.98
Trans-fatty acids					
TFA 18:1	0.68 ± 0.24	0.73 ± 0.27	0.83 ^d	0.81 ^d	0.95
TFA 18:2	0.17 ± 0.02	0.17 ± 0.02	0.10	0.07	0.63
TFA 16:1	0.17 ± 0.04	0.18 ± 0.05	0.78 ^e	0.76 ^e	0.69

^a Adjusted for age

^b p-value for t-test comparing means of tissue samples 20 mg and >20 mg.

^c p<0.05

^d p<0.0001

^e p<0.005

Table 2.

Intraclass correlations and mean coefficients of variation for individual phospholipid fatty acids between participants' triplicate prostate tissue samples.

	Coefficient of Variation	
	ICC ^a	Mean $\pm$ SD ^b
ω -3 fatty acids		
α -linoleic acid (18:3 ω 3)	0.70	0.16 $\pm$ 0.11
EPA(20:5 ω 3)	0.96	0.09 $\pm$ 0.08
DPA(22:5 ω 3)	0.73	0.10 $\pm$ 0.07
DHA (22:6 ω 3)	0.94	0.04 $\pm$ 0.03
Total ω -3 (EPA + DPA + DHA)	0.92	0.05 $\pm$ 0.04
ω -6 fatty acids		
Linoleic Acid (18:2 ω 6)	0.66	0.08 $\pm$ 0.05
Arachidonic Acid (20:4 ω 6)	0.70	0.06 $\pm$ 0.04
Trans-fatty acids		
TFA 18:1	0.87	0.11 $\pm$ 0.08
TFA 18:2	0.28	0.09 $\pm$ 0.06
TFA 16:1	0.81	0.10 $\pm$ 0.08

^aIntra-class Correlation Coefficient; Shrout and Fleiss (1,1)

^bMean of individual participant CV's

Table 3.

Mean Relative Concentrations and correlations of phospholipid fatty acids in plasma and non-malignant prostate tissue

	Correlations			
	Plasm ^a Mean ± SD	Tissue ^a Mean ± SD	Pearson	Partial Pearson ^b
ω-3 fatty acids				
α-linoleic acid (18:3ω3)	0.12 ± 0.03	0.23 ± 0.07	0.03	0.04
EPA(20:5ω3)	0.91 ± 0.51	0.20 ± 0.10	0.93 ^b	0.92 ^b
DPA(22:5ω3)	1.11 ± 0.17	1.00 ± 0.20	0.64 ^c	0.62 ^c
DHA (22:6ω3)	3.85 ± 1.25	2.66 ± 0.54	0.89 ^b	0.89 ^b
Total ω-3 (EPA + DPA + DHA)	5.86 ± 1.70	3.86 ± 0.75	0.90 ^b	0.89 ^b
ω-6 fatty acids				
Linoleic Acid (18:2ω6)	17.13 ± 2.60	7.55 ± 1.02	0.64 ^d	0.69 ^d
Arachidonic Acid (20:4ω6)	12.08 ± 2.08	14.08 ± 1.51	0.58 ^d	0.59 ^d
Trans-fatty acids				
TFA 18:1	1.14 ± 0.45	0.73 ± 0.24	0.89 ^b	0.89 ^b
TFA 18:2	0.16 ± 0.03	0.18 ± 0.02	0.47 ^d	0.42
TFA 16:1	0.29 ± 0.07	0.18 ± 0.05	0.86 ^b	0.85 ^b

^aMean of 3 cores per participant

^bAdjusted for age

p<0.0001

^cp<0.005

^dp<0.05