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Introduction to electrical discharge Plasma

- Plasma: the fourth state of matter consisting of electrons, positive and negative ions, and neutral radicals.
- Plasma generation by electromagnetic field rather than heating gas to high temperature (> 10,000 °K).
- In atmospheric pressure, plasma device have to be small to meet Paschen’s curve.
- RF system requires **impedance matching network** to deliver RF power from generator to the plasma load.
- RF plasma generates **large amount of radicals** in the plasma.
Plasma Chemistry for selective chemical reactions

<table>
<thead>
<tr>
<th>Electron/Molecular Reactions</th>
<th>Atomic/Molecular Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Excitation:</strong></td>
<td><strong>Penning Dissociation</strong></td>
</tr>
<tr>
<td>$e + A_2$</td>
<td>$M^* + A_2$ $\rightarrow$ $2A + M$</td>
</tr>
<tr>
<td><strong>Dissociation</strong></td>
<td><strong>Penning Ionization</strong></td>
</tr>
<tr>
<td>$e + A_2$</td>
<td>$M^* + A_2$ $\rightarrow$ $A_2^+ + M + e$</td>
</tr>
<tr>
<td><strong>Attachment</strong></td>
<td><strong>Charge Transfer</strong></td>
</tr>
<tr>
<td>$e + A_2$</td>
<td>$A^\pm + B$ $\rightarrow$ $B^\pm + A$</td>
</tr>
<tr>
<td><strong>Dissociative attachment</strong></td>
<td><strong>Ion Recombination</strong></td>
</tr>
<tr>
<td>$e + A_2$</td>
<td>$A^- + B^+$ $\rightarrow$ $AB$</td>
</tr>
<tr>
<td><strong>Ionization</strong></td>
<td><strong>Neutral Recombination</strong></td>
</tr>
<tr>
<td>$e + A_2$</td>
<td>$A + B + M$ $\rightarrow$ $AB + M$</td>
</tr>
<tr>
<td><strong>Dissociative ionization</strong></td>
<td></td>
</tr>
<tr>
<td>$e + A_2$</td>
<td></td>
</tr>
<tr>
<td><strong>Recombination</strong></td>
<td><strong>Decomposition</strong></td>
</tr>
<tr>
<td>$e + A_2^+$</td>
<td><strong>Electronic</strong></td>
</tr>
<tr>
<td><strong>Detachment</strong></td>
<td>$e + AB$ $\rightarrow$ $A + B + e$</td>
</tr>
<tr>
<td>$e + A_2^-$</td>
<td><strong>Atomic</strong></td>
</tr>
<tr>
<td></td>
<td>$A^* + B_2$ $\rightarrow$ $AB + B$</td>
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Plasma generates variety of radicals by **direct electron impact reactions** and by **secondary two body collision reactions**.

→ This enables plasma chemistry to achieve selective chemical reactions.

Introduction to Electrosurgery (ES)

- ES employ **Radio Frequency** that neuromuscular stimulation does not occur.
- **Monopolar ES** for tissue removal and **Bipolar ES** for simultaneous vessel sealing and tissue cut.
  - **Ohmic heating (I^2R)** for *cell evaporation and/or denaturation*
    - Usage of Electrical power instead of physical power.
  - **Fast recovery** thanks to less bleeding and smaller incision
    - **Laparoscopy**
    - **Coagulation for bloodless surgery**
# Advantages and Disadvantages of Electrosurgery

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>1. Laparoscopy capability</td>
<td>1. <strong>Large heat damage</strong> on tissue for coagulation</td>
</tr>
<tr>
<td>2. Coagulation capability</td>
<td>2. <strong>Sticking</strong> of electrosurgery device to tissue.</td>
</tr>
<tr>
<td></td>
<td>3. <strong>No selectivity</strong> on different tissue type.</td>
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<tr>
<td></td>
<td>4. <strong>High conduction current</strong> through patient’s body</td>
</tr>
<tr>
<td>Char and its sticking to ES device</td>
<td></td>
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</tbody>
</table>

Proposed Plasma Assisted Electrosurgery to Overcome Major Disadvantages of Electrosurgery

1. Plasma chemical reactions enhancing ES $I^2R$ heating to remove tissue
2. Bladeless plasma jet surgery avoiding tissue sticking to electrode
3. Selective plasma chemistry allows removal of one tissue type and not another underlying or contiguous tissue type.
Illustrative Capacitively Coupled Internal Coaxial Electrode CSU Helium Plasma Jet Device for Skeletal Muscle Tissue Removal

Hypothesis: Plasma chemistry may enhance ES.
- Coaxial plasma with inner and outer electrode.
- Inner electrode as a monopolar ES.
- Plasma jet with $\text{H}_2\text{O}_2$ additive.
- Comparable removal rate and Low heat damage compared to the same power of ES.
Illustrative Capacitively Coupled External Electrode CSU Argon Plasma Jet for Skeletal Muscle Tissue Removal

Hypothesis: Plasma can replace the metal scalpel of current conducting material. At the same time, plasma chemistry may assist ES tissue removal rate as well.

- Argon plasma jet worked as ES to avoid sticking and charring issue.
- Tissue removal rate increased with CCl$_x$ additive.
- Pulsing parameters of pulsing frequency and duty ratio provided knobs to control heat damage and removal profiles.
Illustrative CSU Argon Plasma Jet in water solution for Selective Tooth Whitening Without Toxic Chemical

Hypothesis: Water can be employed as ROS source as well as the cooling agent.

- Plasma jet was created in DI water.
- \( \text{OH}, \text{H}, \text{O} \), and \( \text{H}_2\text{O}_2 \) were produced on the interface of water and the plasma.
- ROS were applied to stain on porcine tooth sample.
- Stain on porcine tooth was completely removed in 10 min. without tooth enamel damage.
Chemically **Reactive Species Created in Rare Gas Atmospheric Pressure Plasmas**

- Mixture of rare gas and feedstock gas
  - $\text{H}_2\text{O}_2$, $\text{CCl}_x$, and $\text{H}_2\text{O}$
- Electrons and rare gas metastables dissociate feedstock gas into radicals
- Reactive oxygen species (ROS)
  - $\text{OH}$, $\text{O}$, and $\text{O}_3$
- **Cl**: Halogen group, the highest electron affinity, the third highest electronegativity, and strong oxidizing agent

Hypothesis: Plasma chemistry may enhance ES in terms of tissue removal rate and heat damage.

- Chicken breast was employed as skeletal muscle sample.
- Comparable tissue removal rate compared to ES.
- Plasma analysis: Dominant OH generation by H$_2$O$_2$ additive
- Study of correlation between OH and tissue removal rate
- Mechanism study by FTIR tissue analysis
Schematic of CSU Plasma Tool #1 and typical operating conditions

- Driven by 13.56MHz
- He plasma with $\text{H}_2\text{O}_2$ entrained from feedstock
- Typical gas flow: He 1000 sccm, $\text{H}_2\text{O}_2$: 16µl/min
- Typical power: 47W
- Stage speed to move the plasma jet across the tissue surfaces in one controlled path: 10mm/sec
Image of tissue removal: Plasma-Assisted ES vs. Pure ES

- Coaxial plasma is a type of device combining plasma with electrosurgery.
  1. Electrical sparks are weak compared to pure ES.
  2. Plasma surrounding the ES electrode.
- Pure ES rely on electrical spark between the electrode and tissue.

He-H₂O₂ plasma vs. Monopolar ES at 47W
Current Waveforms: 
Plasma-Assisted ES vs. Pure ES

**<47W Coaxial plasma irradiation>**

- $I_e^P$: Total current provided to the inner electrode
- $I_t^P$: Current through tissue sample

**<47W Pure Electrosurgery irradiation>**

- $I_e^{ES}$: Total current provided to the electrode
- $I_t^{ES}$: Current through tissue sample

- Pure ES: $I_e^{ES} = I_t^{ES}$
- Coaxial plasma: $I_e^P = I_t^P + I_t^{ES}$
- Coaxial plasma divides the current into plasma generation and electrosurgery.
  → **Less heat generation ($P=I^2R$) of ES process with the same power as Pure ES.**
Tissue removal rate of Pure ES vs. Coaxial plasma

- ES use heat (P=I^2R) to vaporize tissue cells.
- Coaxial plasma divides total power for both of plasma generation and pure ES process.
- However, plasma-assisted ES has comparable tissue removal rate to pure ES.

Therefore,
1. Plasma impinging on tissue surface enhanced ES tissue removal.
2. Tissue removal mechanism of He-H₂O₂ plasma must be different from ES (cell evaporation).
Optical Spectra of He vs. He-$\text{H}_2\text{O}_2$ Plasma

- Powered electrode of pure helium plasma without $\text{H}_2\text{O}_2$ addition sticks to tissue while it does not stick with $\text{H}_2\text{O}_2$ addition. (small removal rate with pure helium plasma)

- Dominant Radicals are $\text{OH}$, $\text{N}_2$, $\text{N}_2^+$, $\text{O}$, $\text{NO}$

- Increased $\text{OH}$ density is the dominant change by $\text{H}_2\text{O}_2$ addition.

He and He- $\text{H}_2\text{O}_2$ coaxial plasma at 47W
**OH Generation by Electron Impact Dissociation Reactions of H$_2$O$_2$ in the Discharge**

<table>
<thead>
<tr>
<th>No.</th>
<th>Reaction</th>
<th>Rate coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Electron impact ionization</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>$e + H_2O_2 \rightarrow OH^+ + OH + 2e$</td>
<td>$2.2 \times 10^{-11}$</td>
</tr>
<tr>
<td></td>
<td>Electron impact excitation and de-excitation</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>$e + H_2O_2 \rightarrow 2OH + e$</td>
<td>$2.36 \times 10^{-9}$</td>
</tr>
<tr>
<td>3</td>
<td>$e + H_2O_2 \rightarrow H + HO_2 + e$</td>
<td>$3.1 \times 10^{-11}$</td>
</tr>
<tr>
<td></td>
<td>Electron impact attachment and dissociative attachment</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>$e + H_2O_2 \rightarrow H_2O + O^-$</td>
<td>$1.57 \times 10^{-10} \cdot T_e^{-0.55}$</td>
</tr>
<tr>
<td>5</td>
<td>$e + H_2O_2 \rightarrow OH + OH^-$</td>
<td>$2.7 \times 10^{-10} \cdot T_e^{-0.5}$</td>
</tr>
</tbody>
</table>

Introduction to Cell, Nucleic Acid, and Lipid Bilayer

- Cell consists of cell membrane, cytoplasm, and nucleus (nuclear membrane and nucleoplasm).
- Cytoplasm and nucleoplasm are protected by membranes made of lipid bilayers.
- **Cell nucleus** contains most of the cell's genetic material, nucleic acids.
- Cytoplasm and membrane of skeletal muscle cell are sarcoplasm and sarcolemma, respectively.
Structure of Skeletal Muscle

- Most of the **sarcoplasm** is occupied by myofibrils, cylindrical bundles of contractile **proteins**.
- Skeletal muscle fibers are **multinucleated**.
- **The nuclei** are dispersed all along the surface of the fibers, just **underneath the sarcolemma**.

Muscle cell membrane damage by plasma-assisted ES may result in nucleus membrane damage.
Cell Membrane Damage by Lipid Peroxidation Induced by OH of Plasma Jet Irradiation

**Mechanism of Lipid peroxidation by OH**

**OH produced from He-H\textsubscript{2}O\textsubscript{2} plasma**

- **Lipids** are a major component of all cell membranes that form lipid bilayers.\[^1\]
- In general, Lipid peroxidation naturally occurs in the body, mainly by the effect of several reactive oxygen species (OH, HO\textsubscript{2}, O\textsubscript{2}^-, H\textsubscript{2}O\textsubscript{2} etc.). HO\textsubscript{2}, O\textsubscript{2}^-, and H\textsubscript{2}O\textsubscript{2} are far less reactive than OH*.\[^2,3\]
- **He- H\textsubscript{2}O\textsubscript{2} plasma jet irradiation provides OH to initiate lipid peroxidation** on muscle fiber membranes of tissue.
- Lipid peroxidation results in **cell damage**.\[^4\]

**Initial reaction of lipid peroxidation:**

\[ \text{Lipid- } H + \text{OH}^* \rightarrow \text{H}_2\text{O} + \text{Lipid}^* \]

4. [N. Jambunathan, Methods in Molecular Biology, 2010, 639, 292]
Hypothesis of Tissue Removal Mechanism by He-H$_2$O$_2$ plasma-assisted ES

- **OH damage of lipid bilayer** *(lipid peroxidation)*
  - Physical weakness and easy rupture of the membranes by electrical spark of ES process or high temperature of the hot electrode.
  - *Rupture of the membranes* expose cytoplasm and nucleoplasm.
  - Electrical sparks of ES **break weak chemical bonds** in cytoplasm and nucleoplasm of skeletal muscle cells.

- **Expected results**
  - OH correlation with tissue removal rate
  - Observation of changes in lipid in membranes, protein in cytoplasm, nucleic acid in nucleoplasm.
  - Observation of different chemical bonds remained after ablation by pure ES and plasma-assisted ES.
    - Sample after plasma-assisted ES may show remained chemical bonds with stronger bonding energies.
  - Protein segments observation
  - Nucleic acid observation outside the ablation groove.
OH Measurement by Emission Spectroscopy
OH Measurement by Absorption Spectroscopy
Strong correlation between OH concentration in the plasma and mass loss of tissue removal

He- H₂O₂ coaxial plasma tissue removal with various power and H₂O₂ flow rate

- OH density and mass loss increase as power increase.
- Both OH density and mass loss are at maximum with about 8μl/min H₂O₂ addition.
- OH density and mass loss track each other.
- Therefore, OH is the dominant species to contribute high tissue removal rate.
FTIR analysis of tissue samples

- Samples to analyze
  1. Control
  2. Effluent gas
  3. Tissue particles in effluent gas
  4. Remaining tissue

- Chemical bond in tissue detected by FTIR
  1. amide A
  2. amide I
  3. amide II
  4. Lipid
  5. Nucleic acid

- Gas phase Chemical bonds detected by FTIR
  1. CO or CO₂
  2. -OH
FTIR analysis of the effluent gas

Chemical reaction of combustion process

\[ C_x H_y + 2O_2 \rightarrow 2H_2O + CO_2 + \text{energy} \ (\Delta E) : \text{exothermic reaction} \]

- **ES** tissue removal process emit CO\(_2\) gas indicating combustion of organic materials.
  - Combustion.
  - Thereby heat generation

- **Coaxial plasma** tissue removal process emit no CO\(_2\) gas.
  - No combustion.

- **ES** tissue removal accompanied combustion and thereby heat generation may cause heat damage on contiguous tissue.
- **Coaxial plasma** tissue removal involved no combustion and thus less heat.
FTIR analysis of remaining tissue in ablation groove

- **ES** showed reduced amide A.
  - **Denaturation** by high temperature.
  - **Heat damage** on the remaining tissue.

- **Coaxial plasma** remained amide A, I, and II.
  - **No denaturation** and thereby less heat damage

- **ES** left remaining tissue denatured by heat.
- **Coaxial plasma** left remaining tissue intact.
Heat damage of ES observed in Masson’s trichrome stained tissue

ES left heat damage on the ablation groove while He-H₂O₂ plasma assisted ES did not leave heat damage.

[Images showing heat damage in Masson’s trichrome stained tissue]

Masson’s trichrome stain:
- Muscle fibers-red, Cartilage-blue/green
- Heat damaged muscle fibers-dark brown
FTIR analysis of filtered tissue particles in the effluent gas

- **ES** remained no chemical bonds in the filtered tissue particles.
  - No chemical bond detected.
  - Filtered particles seems a carbon resulted from carbonization during combustion process.

- **Coaxial plasma** showed no amide A but reduced amide I and II in the filtered tissue particles.
  - Some proteins lost secondary and tertiary structures (**denaturation**).
  - Tissue particles **still remain its original structures**.
  - Protein segments flew away.

- **ES** tissue removal accompanied **carbonization**, outcome of incomplete combustion process that break all of the chemical bonds with excessive heat energy.
- **Coaxial plasma** **mainly broke the weak hydrogen bonds between long chain of proteins**.
Protein Denaturation, Loss of Protein Secondary and Tertiary Structures

- **Protein structures**
  - **Primary**: a series of amino acids by peptide bonds (no change by denaturation)[1]
  - **Secondary** and **Tertiary**: altered by denaturation

- **Amide A, I, and II** represent protein secondary and tertiary structures.[2]

- **Therefore, denaturation** is a process that protein lose the secondary and tertiary structure by application of some external stress (reactive chemical or heat).

Protein Primary Structure

Long chain of amino acids up to 20 are the primary structure of protein.

Protein (polypeptide): protein is a long chain molecule made up of amino acids joined by peptide bonds.
Chemically Weak Hydrogen Bonds Building Secondary and Tertiary Protein Structures

- Hydrogen bonds build up protein secondary and tertiary structures.
- Broke of those hydrogen bonds means loss of these structures and denaturation.

Covalent bond energy
- C-N: 276 kJ/mol
- C-H: 414 kJ/mol
- C=O: 745 kJ/mol
- N-H: 393 kJ/mol

Hydrogen bonds (typical bond energy = 4~8 kJ/mol)

[Gallagher, Warren; "FTIR Analysis of Protein Structure"]
[General Chemistry]
FTIR analysis of periphery and ablation groove

• **Ablation groove:**
  No change in the chemical bonds after removal process.
  → Tissue was removed without damaging or denaturing contiguous tissue.

• **Periphery:**
  1. Large reduction of Amide A
  2. Small reduction of Amide I, and II
  3. Creation of Lipid peaks
  4. Creation of Nucleic acid peaks

• Remained tissue on ablation groove was intact.
• Tissue on periphery was denatured by plasma heat and/or chemicals.
• **Breakage of lipid bilayer** of sarcolemma and nuclear membrane.
• Sarcolemma and nuclear membrane were ruptured.
• Nucleic acids and ruptured membranes (lipids) were spread over the periphery.
Illustrative Capacitively Coupled Internal Coaxial Electrode CSU Helium Plasma Jet Device for Skeletal Muscle Tissue Removal

Hypothesis: Plasma chemistry may enhance ES.
• Coaxial plasma with inner and outer electrode.
• Inner electrode as a monopolar ES.
• Plasma jet with $H_2O_2$ additive.
• Comparable removal rate and Low heat damage compared to the same power of ES.
Mechanisms of tissue removal process by He-\(\text{H}_2\text{O}_2\) plasma-assisted ES

1. He-\(\text{H}_2\text{O}_2\) plasma provided \(\text{OH}\), reactive chemical species.

2. \(\text{OH}\) induced Lipid peroxidation of lipid bilayers consisting of the cell and nuclear membranes. Note that nuclei are just underneath the sarcolemma enclosing the sarcoplasm.

3. Sarcolemma and nuclear membranes become already broken or easy to be broken by lipid peroxidation.

4. ES process after He-\(\text{H}_2\text{O}_2\) plasma exposure easily open the membranes of muscle cells and their nuclei.

5. ES process of He-\(\text{H}_2\text{O}_2\) plasma broke weak hydrogen bonds of secondary and tertiary protein structures due to not enough thermal energy to break strong chemical bonds in the primary protein structure.

6. Nucleic acids in the nuclei and proteins in sarcoplasm are blown away over the periphery.
Conclusion of He- $\text{H}_2\text{O}_2$ Plasma Enhanced Electrosurgery

- Plasma-assisted electrosurgery was developed by generating OH rich helium plasma surrounding ES electrode.
- He-$\text{H}_2\text{O}_2$ plasma enhanced electrosurgery has comparable removal rate to ES with the same power but less current for ES process.
- Strong correlation between OH and tissue removal rate.
- OH radicals in the plasma result in damage on sarcolemma and nuclear membrane.
- Plasma-assisted ES broke weak chemical bonds of secondary and tertiary protein structure (tissue denaturation) but with maintaining the primary structure.
- Protein fragments are blown away in the exhaust gas.
- Rupture of the sarcolemma and nuclear membrane resulted in lipid and nucleic acids spread over periphery.
- No damage by plasma-assisted electrosurgery was observed on the contiguous tissue while combustion and following heat damage were observed with ES.
Hypothesis: Plasma, current conducting material, can replace the metal scalpel of ES. At the same time, plasma chemistry may assist ES tissue removal rate as well.

- Chicken breast was employed as skeletal muscle sample.
- Plasma jet became a conducting material for pure ES eliminating the tissue sticking on the electrode.
- $\text{Cl}_2$, $\text{Cl}$, and $\text{C}$ were generated by $\text{CCl}_x$ additive into the plasma jet.
- Plasma analysis showed that removal rate increases with $\text{Cl}_2$ concentration.
- Pulsed RF parameters of pulsing frequency and duty ratio provided control knobs for removal rate, tissue removal profiles, and heat damage on remained tissue.
Schematic of CSU Plasma Tool #2 and typical operating conditions

- Driven by 13.56MHz power
- Ar plasma with $\text{CCl}_4$ entrained from feedstock
- Typical gas flow: Ar 470 sccm, $\text{CCl}_x$: 20µl/min
- Typical power: 30W
- Stage speed to move the plasma jet across the tissue surfaces in one controlled path: 10mm/sec
Electron Impact Dissociation Reactions of CCl₄ in the CSU Plasma Tool #2

<table>
<thead>
<tr>
<th>No.</th>
<th>Reaction</th>
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<tbody>
<tr>
<td>1</td>
<td>e + CCl₄ → C + 2Cl + Cl₂ + e</td>
</tr>
<tr>
<td>2</td>
<td>e + CCl₄ → C + Cl⁻ + Cl + Cl₂</td>
</tr>
<tr>
<td>3</td>
<td>e + CCl₄ → C + Cl⁺ + Cl + Cl₂ + 2e</td>
</tr>
<tr>
<td>2</td>
<td>e + CCl₄ → C + Cl⁻ + 3Cl</td>
</tr>
<tr>
<td>3</td>
<td>e + CCl₄ → C + Cl⁺ + 3Cl + 2e</td>
</tr>
<tr>
<td>4</td>
<td>e + CCl₄ → C + 4Cl + e</td>
</tr>
<tr>
<td>5</td>
<td>e + CCl₄ → C + Cl⁻ + Cl + Cl₂</td>
</tr>
<tr>
<td>6</td>
<td>e + CCl₄ → C + Cl⁺ + Cl + Cl₂ + 2e</td>
</tr>
<tr>
<td>5</td>
<td>e + CCl₄ → C + Cl⁻ + 3Cl</td>
</tr>
<tr>
<td>6</td>
<td>e + CCl₄ → C + Cl⁺ + 3Cl + 2e</td>
</tr>
</tbody>
</table>
Optical Emission Spectra of Dominant Optically Active **Chlorine** Radical Species

- Dominant Radicals are OH, N$_2$, Cl, Cl$_2$, and C$_2$.
- Increased C$_2$, Cl, and Cl$_2$ density are the dominant change by CCl$_4$ addition.

Optical emission spectra emitted from pure Ar and Ar/CCl$_4$ plasmas
Chicken Tissue Removal by **Chlorine Radicals**

Distinct Cut Profiles as We Vary $x$ in the Different Chlorine Feedstocks $\text{CCl}_x$

Fixed experimental conditions as we vary $x$ in the Chlorine 13.56MHz, RF power: 30 W, tissue treatment speed: 10mm·sec$^{-1}$.

**Side view**

- a. Ar
- b. Ar + CH$_2$Cl$_2$
- c. Ar + CHCl$_3$
- d. Ar + CCl$_4$

**Top view**
Optical Emission Spectra of $\text{Cl}_2$

$\text{Cl}_2$ emission band at 258 nm\textsuperscript{[16,18]} from pure Ar, Ar/ $\text{CH}_2\text{Cl}_2$, Ar/CHCl\textsubscript{3} and Ar/CCl\textsubscript{4} plasmas.

- Addition of CH\textsubscript{2}Cl\textsubscript{2} into Ar plasma did not create noticeable Cl\textsubscript{2} radical.
- CHCl\textsubscript{3} and CCl\textsubscript{4} significantly increased $\text{Cl}_2$ peak intensity.

$\text{Cl}_2$ emission increased as we varied the CCl\textsubscript{x} feedstock as $x$ varies from 2 to 4. This variation of the $\text{Cl}_2$ emission tracks the tissue removal rate.
Histology Samples of Chicken Tissue Following Argon $\text{CCl}_x$ Plasma Jet Irradiation With a Remote Electrode

Histological section of tissue cut using (a) Ar and (b) Ar and $\text{CCl}_4$ plasmas, demonstrating tissue removal enhancement from the chosen reactive plasma chemistry.
Conclusion of the Chicken Tissue Removal by **Chlorine** Radicals

- Pure argon plasma jet works as monopolar ES.
- The cutting depth increased as the number of chlorine atoms in the feedstock molecule increases.
- The lateral etch is not affected by the Chlorine.
- Cutting profile follow the flow of current through the plasma plume, the conductive matter.
FURTHER STUDY of Plasma Jet Tissue Removal driven by Pulsed RF

Pulse operation: high power during ON time
→ more power to excite and generate reactive species such as OH, Cl, O and etc.
→ more power for electrosurgical process. (evaporation of tissue cells)

Power ON and OFF
CW: continuous heat up the sample
Pulse: periodic heat up and cool down

Waveform of Forward and Reflected powers of Pulsed RF plasma
Pulsed RF of ES for Increased Heat Damage

Waveforms for cut, blend, and coag

Increase coagulation  Decrease Heat damage

RF Pulse of Plasma Jet for Reduced Heat Damage

- Significantly reduced char formation of Pulsed RF removal.
- Tissue surface temperature of CW RF (45°C) > Pulsed RF (28°C)
- Therefore, less heat damage with Pulsed RF
Histology samples of CW RF and Pulsed RF treated samples

1. Tissue removal rate is higher with CW
2. More char (dark/brown in masson’s trichrome stained tissue) formation with CW
3. Thicker spongy necrotic layer with CW
Tissue Removal Profiles with Pulsing Frequency and Duty Ratio

150 W peak power 30 Hz

- Both tissue removal area and char formation increased as duty ratio increased from 5 to 30 %. 15 % of duty ratio showed maximized char/removal area.
- The width of the removal profile increased as pulsing frequency increased from 5 to 30 Hz. Removal depth and char formation did not change.

150 W peak power 15 % duty ratio

- Both tissue removal area and char formation increased as duty ratio increased from 5 to 30 %. 15 % of duty ratio showed maximized char/removal area.
- The width of the removal profile increased as pulsing frequency increased from 5 to 30 Hz. Removal depth and char formation did not change.
Conclusion of tissue removal by Pulsed RF plasma

- Duty ratio with given power and pulsing frequency can be optimized for high removal rate with minimal heat damage (carbonization).
- Pulsing frequency with given power and duty ratio can be optimized for removal width.
- Therefore, plasma can be tailored for optimized tissue removal with pulsing frequency and duty ratio.

<table>
<thead>
<tr>
<th></th>
<th>CW</th>
<th>PULSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface tissue temperature</td>
<td>45 °C</td>
<td>28 °C</td>
</tr>
<tr>
<td>Visual char on remaining tissue</td>
<td>Exist</td>
<td>None</td>
</tr>
<tr>
<td>Removal area (or rate)</td>
<td>Large</td>
<td>Small</td>
</tr>
<tr>
<td>Necrotic area</td>
<td>Thick</td>
<td>Thin</td>
</tr>
</tbody>
</table>
Future work

• Investigate selectivity of plasma chemistry removal of different tissue types
  – Relative selectivity studies of heart, lung, kidney, muscle, and liver tissues

• Investigate selectivity of plasma chemistry removal with different chemical feedstock and plasma conditions.

• Relation between radical densities and etch profile and/or mass loss.

• Pulsed RF plasma with different chemical feedstock.

• Mechanism study of remained and removed tissue samples
  – Toxic effects of CCl₄ on the liver caused by lipid peroxidation.[1]
    
    CCl₄ → CCl₃⁻ (metabolization by the cytochrome P-450 system in liver)
    
    CCl₃⁻ + O₂ → CCl₃O₂⁻ (react rapidly with oxygen in liver)
    
    Lipid-H + CCl₃O₂⁻ → A Lipid radical + CCl₃O₂H (lipid peroxidation)

Future Tooth Whitening Without Dangerous Radicals or Feedstocks by *In-situ* Generation of Reactive Radicals From Benign Feedstocks

Hypothesis: Water can be employed as ROS source as well as the cooling agent.

- Advantages and disadvantages of $\text{H}_2\text{O}_2$ conventional tooth whitening
- Ar-water feedstock creating plasma contains OH
- $\text{H}_2\text{O}_2$ free water plasma generation of OH
- OES of the Ar-water plasma
- Removal of stains on tooth surfaces vs. Ar-water plasma irradiation time
- Low damage to tooth enamel after plasma based stain removal
Problems of Conventional Tooth Whitening with $\text{H}_2\text{O}_2$

Still need more treatment time

(a) 1 cycle  (b) 2 cycle  (c) 3 cycle  (d) 4 cycle  (e) 5 cycle  (d) 6 cycle

1 cycle: 1 min soaking in the 30 wt% $\text{H}_2\text{O}_2$ solution
Advantages and Disadvantages of Conventional $\text{H}_2\text{O}_2$ Tooth Whitening

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Simple</td>
<td>1. Toxic chemical (high concentration of $\text{H}_2\text{O}_2$)</td>
</tr>
<tr>
<td>2. Inexpensive</td>
<td>2. Long treatment time (at least 30 min in general)</td>
</tr>
<tr>
<td></td>
<td>3. Damage on enamel by $\text{H}_2\text{O}_2$ (low selectivity of the chemical etching)</td>
</tr>
</tbody>
</table>

Ar-Water Feedstock Creating Plasma Containing OH
Stain on tooth was removed in 8 min of plasma treatment.
Low Damage to Tooth Enamel After Plasma Based Stain Removal

Stain on the tooth surface was completely removed without damage on enamel after 10 min plasma treatment at 30 W.
Optical Emission Spectrum of The Argon-Water Plasma

- Dominant radical species are \( \text{OH} \) and \( \text{O} \).
- Plasma temperature is about to 2000K (\( \approx 1700^\circ \text{C} \)).
- However, the water temperature where the samples of tooth locate (3mm below the termination of plasma jet) was 35 ± 5°C.

=> No contact of plasma but contact of delivered chemicals in the bubbles.
Maximization of \( \text{OH} \) with Minimized \( \text{H}_2\text{O}_2 \)

- \( \text{OH} \) is the dominant species produced by the plasma.
- \( \text{H}_2\text{O}_2 \) concentration is kept lower than 2 \( \mu \text{M} \).
- Therefore, cell damage by \( \text{H}_2\text{O}_2 \) is prevented since it is less than 30 \( \mu \text{M} \), the minimum level for soft tissue cell death).

\[
\text{H}_2\text{O} \text{ decomposition} \\
e + \text{H}_2\text{O} \rightarrow \text{H}^+ + \text{OH}^- + e \\
e + \text{H}_2\text{O} \rightarrow \text{O} + \text{H}_2^+ + 2e
\]

\[
\text{H}_2\text{O}_2 \text{ Generation} \\
2 \text{OH} \rightarrow \text{H}_2\text{O}_2 \\
2 \text{HO}_2 \rightarrow \text{H}_2\text{O}_2 + \text{O}_2
\]

\[
\text{HO}_2 \text{ Generation reaction} \quad [\text{cm}^3/\text{sec}] \\
e + \text{H}_2\text{O}_2 \rightarrow \text{H} + \text{HO}_2 + e \\
\text{OH}^- + \text{O} \rightarrow \text{HO}_2 + e
\]

\[
\text{OH} \text{ Generation} \\
e + \text{HO}_2 \rightarrow \text{OH} + \text{O} + e \\
e + \text{H}_2\text{O}_2 \rightarrow 2\text{OH} + e
\]

The fastest reaction

- \( \text{H}_2\text{O} \) decomposition
  - Rate Coefficient function of \( P_{\text{plasma}} \)
  - \( 3.1E-11 \)
  - \( 2E-10 \)

- \( \text{H}_2\text{O}_2 \) Generation
  - Rate Coefficient
  - \( 1.1253E-12 \)
  - \( 1.15E-11 \)

- \( \text{HO}_2 \) Generation reaction
  - Rate Coefficient
  - \( 3.1E-11 \)
  - \( 2E-10 \)

- \( \text{OH} \) Generation
  - Rate Coefficient
  - \( 1.67E-09 \)
  - \( 2.36E-09 \)
pH Measurement of The Plasma Treated Solution

\[ H_2O + CO_2 \leftrightarrow H_2CO_3 \]
\[ H_2CO_3 \leftrightarrow HCO_3^- + H^+ \]

pH of the DI water become less than 7.

- pH decrease as \([H^+]\) increase. (pH = \(-\log_{10}[H^+]\))
- \([OH^-]\) increase with increasing \([H^+].\) (\(H_2O \leftrightarrow H^+ + OH^-\))

\[ e + H_2O \rightarrow H^+ + OH^- + e \]
\[ e + H_2O \rightarrow O + H_2^+ + 2e \]

\[ pH = -\log_{10}[H^+] \alpha \frac{1}{[H^+]} \]
Measured and Calculated Electrical Conductivity of The Plasma Treated Solution

\[ \sigma = -\rho_-\mu_- + \rho_+\mu_+ \]

\( \rho_- \): charge density of \( \text{ion (OH}^-\text{)} \)
\( \mu_- \): mobility of \( \text{ions} \)
\( \rho_+ \): charge density of \( \text{+ion (H}^+\text{)} \)
\( \mu_+ \): mobility of \( \text{+ions} \)

Conductivity \( \alpha \frac{1}{[pH]} \)

- Measured electrical conductivity and the calculation from measured pH value agree each other.
- Both \( \text{H}^+ \) and \( \text{OH}^- \) contribute to the electrical conductivity.
- Therefore, \( \text{H}^+ \) and \( \text{OH}^- \) are the dominant ion species in the solution.
Low Water Temperature Prevention by Thermal Damage

Water temperature measured 3 mm below of the plasma plume.

• Thermal plasma decomposed $\text{H}_2\text{O}$ and generated reactive species such as $\text{OH}^-$ and $\text{H}_2\text{O}_2$.

• The high temperature prevention by water cooling.

• The water temperature is under 40 °C.

Therefore, the thermal damage on the soft tissue surrounding teeth was ignorable, while keep generating reactive species with thermal plasma at the interface of plasma and water.
Conclusion of tooth whitening with hybrid water-gas plasma jet

- Argon-water plasma jet dominantly created OH.
- $\text{H}_2\text{O}_2$ concentration $< 2 \mu\text{M} (< 30 \mu\text{M},$ the minimum limit of soft tissue cell death)
- OH removed tooth stains with selectivity of stain to tooth enamel.
- Water temperature on the location of the teeth sample was kept under 40 °C similar to body temperature while the plasma temperature was about 2000 °K.
- Tooth whitening of 30 W argon-water plasma jet was achieved typically in 10 min.
- High Selectivity is demonstrated in removing stains but not removing tooth enamel.
Plasma Biomaterial Selective Interaction
Conclusions and Identified Pathways to Future Studies via Preliminary Work

• Monopolar electrosurgery can be enhanced by atmospheric plasma.
  – **OH** radicals have a role to enhance the removal rate.
  – Plasma assisted ES left less heat damage on remaining tissue.

• Bladeless(non-contact) electrosurgery was achieved using atmospheric plasma jet.
  – Chemical feedstock $\text{CCl}_x$ additives placed into the discharge enhanced tissue removal rates.
  – Pulsed RF plasma enhanced tissue removal in terms of heat damage on the contiguous tissue.

• High Selectivity is demonstrated in removing stains but not removing tooth enamel.
Future work for RF plasma application to biomedical

- Mechanism studies of the plasma chemistry of selective reaction with biomaterials.
  - Selective removal of various tissue.
- Understanding and Development of independent control knobs for selective radical generations.
  - Concentration of feedstocks
  - Power, voltage, current, and etc.
- Maximize desired plasma chemistry using the developed control knobs.
  - Plasma can be tailored for each applications.
Thank you